

REVIEW

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Treatment of skin metastases of breast cancer

Introduction

Although skin metastases of breast cancer are visible, palpable and therefore a bothersome burden to the patient in the psychological and more often in the physical sense by pain and need of care, bandages, foul smell, etc., the paucity of data about incidence and treatment surprises the interested oncologist. Results of treatment are difficult to find, and data on incidence are not easily found in the medical literature. Textbooks on cancer treatment neglect the subject, and literature data found in journals are only sparse.

Incidence

In an article in the *Journal of the American Academy of Dermatology*, Lookingbill et al. [1] published a retrospective analysis of their findings in cutaneous metastases of cancer. In their database comprising 4020 patients with metastases, they found 300 female and 400 male patients overall with skin metastases. Of the female patients, 70.7% had metastases of breast cancer in contrast to only 2.4% of male patients. In melanoma 12% of female patients and 32.3% of male patients had skin metastases. Only 3.3% of women with cancer of the ovary had skin metastases, which were more often found in male patients suffering from colorectal cancer: 11.2% of 127 patients.

Focusing on skin metastases of breast cancer, they found that the site of metastases was the scalp in 13.5% of their breast cancer patients, the face in 22.2%, the

neck in 9%, the chest wall in 39%, the abdominal wall in 15% and other localisations in 30.5%. One very rare site of metastases should be mentioned out of interest: carcinomatosis blepharitis, in my own experience 4 patients, inflicting the lower eyelid and causing painful eyes.

Manifestations

Skin metastases in breast cancer patients are manifested in several, sometimes diabolic, ways. They may manifest themselves by single subcutaneous nodes, single intra-cutaneous lesions (Paget type), multiple subcutaneous or intercutaneous lesions, cancer en cuirasse involving the whole chest wall and sometimes by rapidly progressive necrotic ulcerating lesions. This description falls short in describing the discomfort, anxiety and suffering of patients with skin metastases of breast cancer. On the other hand, pictures are too easily found, doomed to exaggerate the clinical spectre.

Treatment

Considering the treatment of skin metastases of breast cancer, again one is confronted with a paucity of data. In particular, study results seem to be lacking, and traditional treatment policies are followed. Surgery, radiation and systemic hormonal and/or chemotherapy are applied. Within the radiotherapy literature, the focus is mainly on local, relapsing recurrences involving the skin. One should define the treatment modalities into: (1) surgery with or without radiotherapy, (2) radiotherapy, involving brachytherapy and hyperthermia, (3) photodynamic therapy, and (4) chemotherapy, applied systemically or locally.

Surgery

It seems to be simple to excise a local recurrence or a skin metastasis of breast cancer. Attending surgeons

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should, however, realise that maybe such a skin metastasis is the sole evaluable (e.g. measurable) lesion of a breast cancer patient with far more metastasis. Therefore, after cytologically given proof of metastases, further staging procedures should be performed, e.g. bone scan, x-ray of the chest, liver ultrasound, before excision. Skin metastases of patients in the breast cancer clinic should always be discussed in a multidisciplinary team.

In a classic publication, Fentiman [2] showed that the prognosis of patients found to be suffering from skin metastases of breast cancer depended largely on the incidence of more advanced disease. In patients found to have single cutaneous lesions, a 42% 5-year survival and a 22% 10-year survival could be documented in a retrospective analysis of more than 200 patients, while patients suffering from metastases in multiple organs at the occurrence of skin metastases had a 10-year survival rate of 0% and only 10% of the patients survived 5 years.

This is one more important argument to support *local* control of skin metastases if only this organ is found to be afflicted by breast cancer.

Radiotherapy

Again, paucity of data overwhelms the surveyor of the literature. According to an authority in radiotherapy, the past chairman of the radiotherapy group of EORTC, many radiotherapy regimens are in use in the treatment of skin metastases (after excision) (H. Bartelink, personal communication). Regimens consist of 1×8 Gy, 3×8 Gy, 5×3 Gy, etc. (no comparative studies have been done).

The aggressiveness of the palliative radiotherapy regimen and the use of radiation ports of the whole operation field seem to be related to the time elapsed since the primary curatively intended treatment, e.g. radiotherapy or previous radiation treatment. For example, a skin metastasis manifesting itself within 2 years of previous surgery could be a seeding metastasis (although arguments are to be found that these are primary manifestations of systemic disease), and radiation of the whole operation field could be considered after removal of such a (scar) metastasis.

The problem becomes more difficult when such a metastasis in the operation field occurs after primary surgery including radiotherapy. Treatment of these skin manifestations of breast cancer occurring in the operation (radiation) field calls for local treatment by either radiotherapy or photodynamic treatment. The occurrence of such local recurrences in the skin even with a treatment-free interval of more than 27 years (personal experience) should be mentioned. The role of radiation treatment should be defined further in prospective studies.

Vernon et al. [3] showed that the combination of hyperthermia and radiotherapy, although difficult to analyse since local occurrence in the breast not inflicting

the skin has been treated in the same way, results in better local control at 3 years in previously radiated lesions in 40 versus 20% of the patients treated with radiation alone.

Photodynamic therapy

Photodynamic treatment (PDT) so far falls short for final evaluation. The data so far are based on small series of patients treated with photosensitizing agents and laser lightening of skin metastases. Personal experience with this treatment modality, still to be regarded experimental points to a high anti-tumour efficacy at the cost of tolerable local toxicity (necrosis) and systemic side effects, since patients are to be kept away from sunshine for at least 1 week. Newer sensitising agents are currently being developed.

Systemic treatment

Systemic treatment, be it hormonal treatment or toxic chemotherapy, could be considered in these patients as well. The addition of "adjuvant chemotherapy" to local treatment of a locally recurring breast cancer has not been defined, an EORTC study even had to be aborted. So far no argument can be found in the literature to add systemic hormonal or chemotherapy to the treatment of local recurrences or a sole skin metastasis in the operation and/or radiation field.

Overall, skin metastases seem to react maybe slightly better than liver or lung metastases to hormonal therapy and/or chemotherapy.

Local treatment with cytostatic agents

Based on the publication of Fentiman [2], the majority of patients with manifesting skin metastases will suffer from multiple organ metastases during time, e.g. further skin metastases, lung, liver, bone/metastases. Therefore, postponement of systemic treatment in order to delay toxic chemotherapy in these patients should be considered, as curative strategies for patients with metastasised breast cancer are only limited, if at all available [4].

Local treatment by radiotherapy and surgical excision, as mentioned above, should be advocated, as should application of local treatment with PDT and locally applied chemotherapy. Locally applied chemotherapy may involve miltefosine treatment of skin metastases. Miltefosine is a protein kinase C inhibiting agent, inhibiting the signal transduction of growth factors to nucleus, which has not been proven to be feasible by i.v or oral route. Therefore a local application route has been developed.

Local application results in a shrinkage of skin metastases even in far advanced (breast cancer) cases of about 30% for a median duration of 6 months. Side

effects are minimal: only if the treated areas of skin metastases are more than 10×10 cm nausea and vomiting have been reported; skin irritation and desquamation are seen as side effects otherwise. Further studies with this attractive treatment modality should be advocated.

References

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