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"Extensive" T4 breast tumors: Considerations regarding local management.

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Abstract

"Extensive" T4 malignant breast tumors are not uncommon and can be either primary or recurrent. Theycan present without or be accompanied by distant metastases at the time of initial presentation. They share one or more of the following symptoms: mass effect, pain, malodor, esthetic distress, exudation, pruritus, bleeding, and crusting. The aim of their treatment is therapeutic, when possible, or palliative, which is quite often the case. A small case series of three female patients with "extensive" T4 breast cancer is presented. The various surgical options for excision of the tumor and reconstruction of the resulting defect are discussed. Methods of management of odor, infection control, and pain, especially when surgery or radiotherapy is contraindicated, is also discussed.

Key words: Extensive T4 breast cancer, malignant wounds, fungating breast lesions, locally advanced breast cancer, chest wall defects, reconstruction, reverse abdominoplasty, pedicled flaps, free flaps, absorptive dressings, topical antibiotics, bone metastases, peripheral nerve blocks.

Introduction

The latest (2017) Cancer Staging Manual[1] of the American Joint Committee on Cancerdefines T4 malignant breast tumors as the tumors of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules); invasion of the dermis alone does not qualify as T4. The four subcategories are:

T4a: Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of chest wall structures does not qualify as T4.

T4b: Ulceration and/or ipsilateral macroscopic nodules and/or edema (including peau d' orange) of the skin that does not meet the criteria for inflammatory carcinoma.

T4c: Both T4a and T4b are present.

T4d: Inflammatory carcinoma.

Unfortunately, neither the extent of chest wall invasion (T4a) nor that of skin ulceration (T4b) is elab-

orated in the latest(8th) edition of the Cancer Staging Manual. In reality, however, T4lesions can reach considerable dimensions, regardless whether they are primary or recurrent. Overwhelming physical and psychological symptoms like pain, malodor and bleeding may affect women with such "extensive" T4 malignant breast tumors, resulting in a poor quality of life and a significant impact on one's self-image.

Wide surgical resection and use of advanced reconstructive techniques for the large defectsof the chest wall and skin, either in the curative or the palliative setting, can relieve the patient from the afore mentioned symptoms. In selected cases, the loco regional progression-free survival (PFS) and even the overall survival (OS) are prolonged. When surgery is not possible, due to the patient's poor performance status, palliative management of pain with local analgesia and opioids improves the quality of life. Fungating lesions can be treated using radiotherapy[2,3], new dressings and even old techniques such as larval therapy[4].

Aim of this article is to report a small case series of three patients with "extensive" T4 malignant breast tumors, discuss the treatment options and review the relevant literature.

Patients and Methods

From January 2017 to December 2018, three patients were referred to the author because of an "extensive" T4 breast cancer. The patients, all female had a mean age of 76, 6 years (range, 55-95) at the time of the initial consultation. The right side was affected in one and the left side in two patients. There was a primary tumor in one patient and a recurrence of previously treated tumors in the remaining two patients. One of the neoplasms was classified as cT4a, one as cT4b and one as pT4b. One patient underwent a wide surgical resection and reconstruction. Poor performance status of the other two patients (Karnofsky score 60and 50 respectively, both ASA III) did not allow surgery, and therefore both of them were managed with a palliative intent. Follow-up ranged from 6-24 months. One patient (surgery) is still alive with no evidence of local disease. One patient was lost to follow-up and another succumbed to her disease.

Case reports

Case1

A 42-year old female patient was operated elsewhere because of a 2.2 cm malignant neoplasm of the left breast. A total mastectomy with axillary clearance was performed. According to the histopathological report the tumor was a moderately differentiated, invasive ductal carcinoma which developed on the basis of a 0.8 cm benign fibroadenoma. Elements of an in situ carcinoma (ethmoid type) were also identified in the surgical specimen. Four out of the 24 removed lymph nodes presented malignant neoplastic ingrowth. The tumor stained positive for estrogen receptors (ER-18%), progesterone receptors (PR-55%) and HER-2 (score 3+). Adjuvant chemotherapy, radiotherapy, hormone therapy and trastuzumab (Herceptin) were administered. The patient remained disease free for eight years, after which a solitary liver metastasis was diagnosed, which was treated with adjuvant chemotherapy. In 2015 she presented with a small ulcerative lesion on the chest wall practically on the previous mastectomy scar. Little attention was initially paid by the treating physicians. Later, as the ulcer kept growing, an incisional biopsy was taken. Histopathological examination revealed a recurrence of the invasive ductal carcinoma. For unclear reasons, no surgical excision was considered and the patient was put on a new chemotherapeutic regimen. The latter proved ineffective and the ulcerative lesion continued increasing in size. In 2017 the author was consulted regarding a large malignant wound on the left chest wall. Clinically there was an extensive, malodorous, seeping, ulcerative lesion of the anterolat-

Figure 1. Malodorous, seeping, ulcerative lesion of the anterolateral chest wall in patient 1.

eral chest wall (Fig. 1). The MRI and the bone scan suggested that rib invasion was quite unlikely (cT4bN0M1). Wide surgical resection was decided upon and carried out under general anesthesia (Fig.2). The frozen section of the excised periosteum of the 5th, 6th and 7th ribs showed no tumor invasion and rib resection was considered unnecessary. The large soft tissue defect (25x20 cm) (Fig.3) was reconstructed with a reverse abdominoplasty flap (Fig. 4). The post-operative coursewas uneventful. The excised neoplasm was diagnosed as a poorly differentiated invasive ductal carcinoma of the breast, type not otherwise specified (NOS), grade 3 (Nottingham system).The resection margins were free of tumor.The tumor cells stained negative for ER and PR, and strongly positive for c-erb-2 (3+).The patient was put on adjuvant chemo/immunotherapy (Taxanes,Pertuzumab-Perjeta) and continued the trastuzumab. Clinical and radiological follow-up at 3, 6, 12, 18 and 24 months showed no signs of local recurrence. It is worth noting that the solitary liver metastasis showed a considerable remission after surgery (3.2 cm to 2 cm). It increased back to 3 cm 15 months postoperatively, for which the medical regimen was adjusted (Trastuzumab/Emtasine-Kadcyla). It remains unchanged since then and the patient, still under medical treatment, is alive and well with disease (the liver metastasis).

Case 2

A 92-year old female patient consulted the author because of a long lasting neoplasm of the right breast. A previous incisional biopsy showed a well differentiated invasive ductal carcinoma. The patient initially refused any kind of treatment. With time, however, the neoplasm invaded the overlying skin, the fungating skin surface became contaminated and malodorous and the local pain necessitated the administration of analgesics. Thus far she had been managed with frequent change of dressings and systemic analgesics. On clinical examination the entire right breast was a fungating, malodorous tumor mass (Fig. 5). The patient suffered from a severe heart failure and had a Karnofsky Performance Score

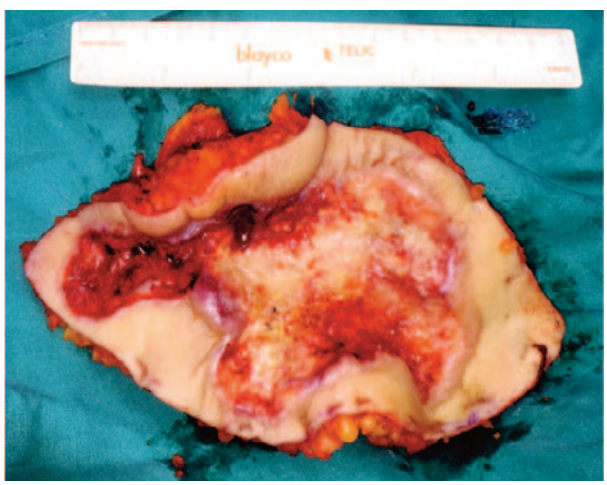

Figure 2. The resected specimen of the ulcerative chest lesion in patient 1.

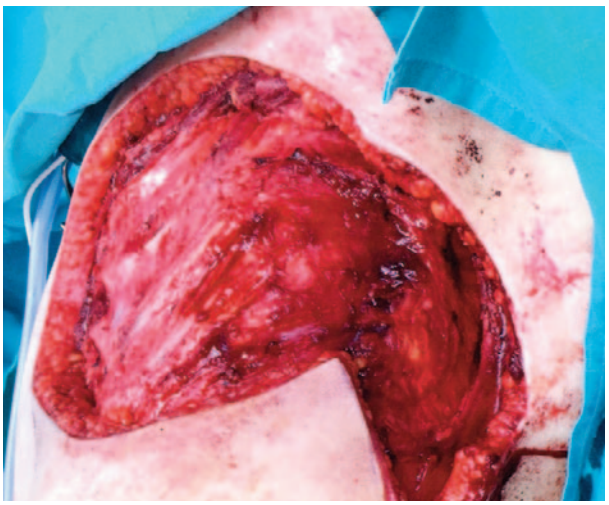

Figure 3. The soft tissue defect of the anterior chest wall in patient 1.

of 50 (ASA physical status III). Her Performance Status was an absolute contraindication to any surgical or radiotherapeutic treatment. There was no indication for staging procedures, as the patient would not receive any medical treatment either. Instructions regarding local wound care (twice daily disinfection with Povidone-Iodine solution 10%, Hydrogen Peroxide solution 3% and finally Sodium Chloride 0.9%; application of topical antibiotics –metronidazole 0.8%; and dressing -fatty gauze, gauze impregnated with Povidone-Iodine 10%)were given to the district nurse; administration of systemic analgesics was to be continued.The malodor and local pain improved considerably after the first week of treatment. The patient was lost to follow-up.

Case 3

An 80-year old female patient consulted the author because of a painful lump on the sternum. She reported a previous (14 years previously) history of a pT2N1M1 invasive ductal carcinoma of the left breast, for which a left modified radical mastectomy and left axillary clearance had been performed. Adjuvant chemo/hormone therapy had also been ad-

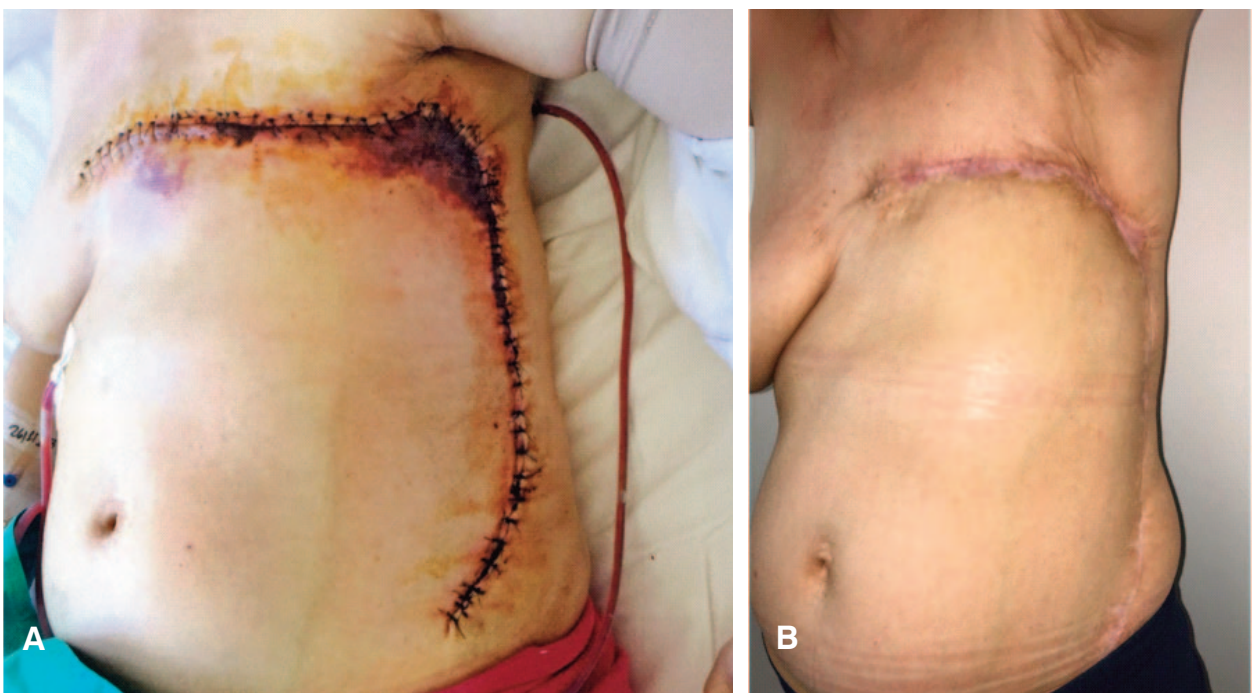

Figure 4. **A**. View of patient 1 three days postoperatively. **B**. The same patient 18 months later.

Figure 5. The right breast of patient 2 was a fungating, malodorous tumor mass.

ministered. It should be noted that a year later she presented with a serous carcinoma of the ovary for which she was treated with surgery and adjuvant chemotherapy. Twelve years after the initial breast treatment, the patient presented a small lump on the sternum. Surgical excision was excluded, due to her poor Performance Status and merely a diagnostic incisional biopsy was performed, the result of which was: recurrent invasive ductal carcinoma of the breast. The patient was treated with radiotherapy and additional chemotherapy. An initial response to treatment was noticed, however, the lump recurred with severe pain in and around the sternal area. Systemic analgesics plus "maintenance"chemotherapy were administered, however, the cancer pain became refractory to systemic analgesics, even opioids (morphine).On presentation, a firm/hard lump was noticed on the patient's sternum (Fig. 6). On the CT-scan, the neoplasm was easily identifiable; it had invaded the sternum causing a pathological fracture and was protruding into the thoracic cavity (Fig. 7). Distant metastases were present in the thoracic part of the vertebral column. Surgical resection of the lump and partial sternectomy followed by sternal reconstruction was absolutely contraindicated due to the patient's poor Performance Status (Karnofsky Performance Scoreof 50, later of 40). In order to alleviate the local pain symptoms and reduce the systemic analgesics, administration of local analgesia was decided upon. Infiltration of the 2nd, 3rd, and 4th intercostal nerves bilaterally adjacent to the sternocostal angle with a solution of procaine (Puren, Pharma GmbH, Muenchen, Germany) and betamethasone (CelestoneChronodose, Merck Sharp & Dohme, AΦBEE, Greece) was performed. A total of 3 ampsPuren (20mg/ml, 5ml) and two vialsCelestoneChronodose (3mg/ml, 1ml) divided into six equal doses were utilized. The pain intensity decreased from numerical rating scale 6 to 7 to 2 to 3 at rest, and from 10 to 4 to 5 of breakthrough pain. Use of systemic analgesia was significantly reduced to oral intake of paracetamol (Depon, Bristol-Myers-SquibbAE, Greece) up to a maximum dose of three

Figure 6. A firm/hard lump was noticed on the cranial part of the sternum of patient 3.

tablets daily (1000mg/tab). Opioids were used only occasionally. The procedure was repeatedevery fourth week, the procaine having been replaced with bupivacaine. The patient, unfortunately, succumbed to her disease six months later.

Discussion

Malignant tumors of the breast invading the skin have been designated as T4b and the ones invading the chest wall as T4a by the American Joint Committee on Cancer (AJCC-Cancer Staging Manual 2017)[1].However, there is still confusionamong authorsregarding terminology. Various authors use different terms like malignant wounds[5, 6, 7], fungating breast lesions[8] or locally advanced breast cancer (LABC)[2, 9] to describe T4b breast tumors. It should be noted, that the latter(LABC) is the mostperplexing. Recent guidelines from the U.S. National Comprehensive Cancer Network (NCCN) define LABC as AJCC Stage III breast cancer, meaning breast cancer which fulfills the following criteria: tumors > 5cm with regional lymphadenopathy, tumors of any size with extension to the chest wall or skin, presence of regional lymphadenopathy regardless of tumor stage, all in the absence of distant metastasis[10]. The afore mentioned authors[2, 9] have used the term LABC, and so have all others whoused the terms malignant wounds or fungating lesions, for patients with T4a and T4b breast cancers without, as well as with metastatic disease on presentation.We complied with the AJCC T4 designation adding the adjective "extensive" in order to better illustrate the true nature and local extent of these neoplasms.

Regardless of the term, these breast tumors, primary or recurrent, with or without distant metastases on presentation, are not uncommon even in the Western developed societies. Although not as prevalent as before (Fig. 8), 5-10% of tumors, particularly in breast cancer, are expected to fungate[6].These tumors share one or more of the following symptoms: pain, mass effect, esthetic distress, exudation, odor, pruritus, bleeding, and crusting[6]. Malodorous and oozing wounds also trigger anxiety about seepage, prevent women from wearing feminine attire and cause them to suppress the need for physical closeness and sexual activity[5], as was experienced by the first and second patient of the present study. Fromantin et al[7] reported that most of these extensive tumors are invasive ductal carcinomas.

The prognosis of these patients is not favorable. A 5-year survival rate of 30-40 % has been reported[9, 11]. Regardless of the prognosis, however, the devastating impact of the symptoms on the patient's quality of lifenecessitates some form of management. Initially, systemic therapy (chemotherapy, immunotherapy) fol-

Figure 7. CT scan of the thorax of patient 3 showing bone invasion and a pathological fracture of the sternum.

lowed by surgical resection whenever the patient's performance status is not a contraindication, is the preferred mode of treatment. From the surgical point of view, contemporary management of T4 breast cancer includes mastectomy andaxillary dissection (or eventuallysentinel node surgery)[12]. Surgical excision of extensive T4 breast cancers results in large tissue defects, which is itself a drawback for many surgeons. Improvement in the use of reconstructive techniques (reverse abdominoplasty, regional flaps, and free flaps) gives the surgeonthe possibility to undertake wide resection of large tumors, often with therapeutic intent (negative surgical margins), which would otherwise have been considered 'unresectable'.

Some authors have considered LABC a contraindication to reconstruction[13]. Recent studies, however, demonstrated that cancer relapse rates are similar between LABC patients treated with and without immediate reconstruction[14].

Full thickness upper anterior/anterolateral (central) trunk defects following oncological resection present indeed a reconstructive challenge. Full thickness defects of the chest wall require close cooperation of the cardiothoracic and reconstructive surgeons to achieve an optimal outcome and reduce the complication rate. Reconstruction of the former includes management of the pleural cavity and skeletal support, must preserve long term function and should not be a hindrance to adjuvant radiotherapy[15]; these goals are achieved with several techniques, using alloplastic materials (methyl methacrylate based customized plates or neo-ribs, osteosynthesis systems or dedicated prosthesis, polypropylene mesh) [16,17] and more recently biologic mesh (swine dermal collagen prosthesis)[18], autografts and homografts[19]. A biologic mesh would have been our choicein patient 3, if her performance status would have permitted us to resect the chest wall recurrent tumor including the fractured sternum. The future of chest wall reconstruction may lie with absorbable semi-rigid meshes, biointegratable acellular homografts and xenografts, demineralized bone matrices and bone marrow stromal cells or the patient's own lab-grown stem-cell based vascularized osteomyocutaneous chest wall grafts[19].

Next step in the chest wall reconstruction ladder is cover of the soft tissue defect. Various algorithms have been proposed to aid a systematic approach, however, the appropriate choice remains very much patient-dependent[15, 20, 21]. Local, pedicled or free flaps have been described to serve this reconstructive purpose. Local

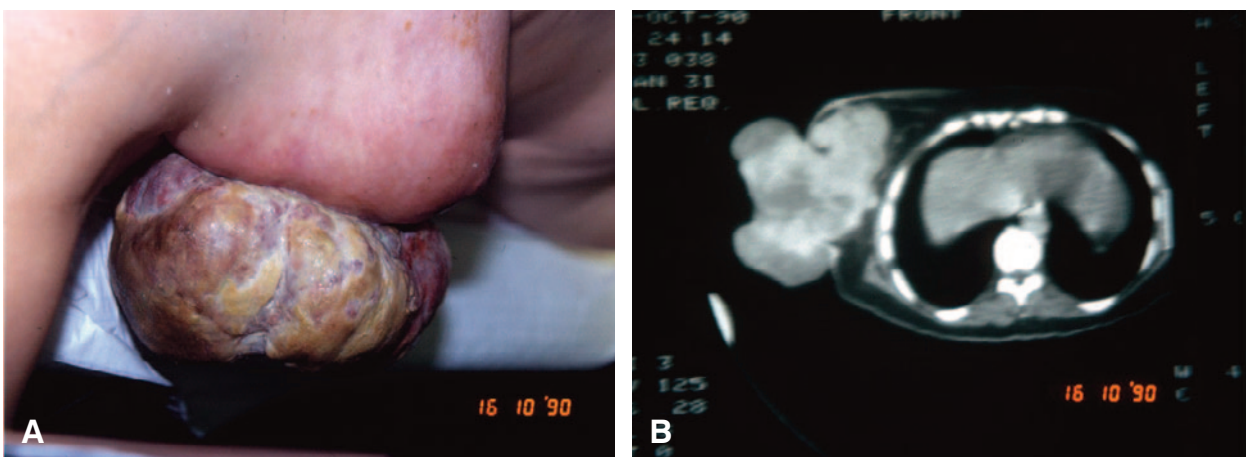

Figure 8. **A**.A large, fungating mass of the right breast in a 55-year old female patient (from the author's previous, West European experience). **B**. CT scan of the same patient. The mass is clearly identifiable.

flaps may be unavailable, whereas flap viability may be compromised by previous or planned chest wall radiotherapy[22]. Pedicled myocutaneous flaps have been successfully utilized by several authors. The transverse rectus abdominis myocutaneous (TRAM) and the latissimus dorsi myocutaneous (mc) flap have traditionally been recommended for cover of these large defects[23, 24]. The former has been reported to be more suitable for medial upper trunk lesions, whereas the latter is considered a first-line option for more lateral defects at this level[23]. The conventional design of the latissimus dorsi mc flapwith skin islands more than 12 cm wide occasionally requires skin grafts for the closure of donor sites[25]. Normally, this limitation occurs in patients who have insufficient dorsal elasticity or in very thin patients. It can be overcome using a different design, the so called extended V-Y latissimus dorsi mc flap, which enables primary closure of the donor site in a V-Y form[26]. Defects up to 34 cm long and 27 cm wide can be thus covered; the complication rate has been reported quite low (flap 8%-seroma 12%)[13]. When the latissimus dorsi mc flap is planned, a careful evaluation of the patency of its vascular pedicle, the thoracodorsal artery and vein, should be performed in the axilla and the lateral thoracic area. In the presence of extensive undermining of these regions with thoracodorsal vessel lesions, the method is contraindicated.

Complex defects, which cannot be covered with local tissues due to severe damage or pedicled flaps due to insufficient size or reach, may require free tissue transfer[27]. The rectus abdominis myocutaneous flap (free or supercharged)[27] and the anterolateral thigh (ALT) free flap[28] have been used for this purpose. A 100 percent success rate and a 15% of perioperative deaths due to multisystem failure have been reported[27] after use of the rectus abdominis. The superior blood supply is an advantage of free flaps; however, the longer operative time and the possibility of total flap failure are disadvantages which ought to be considered[22].

The reverse abdominoplasty offers a good alternative to pedicled or free flap reconstruction. It was first described by Baroudi et al[29] combined with mammary reduction. It has since been infrequently reported mainly as an aesthetic procedure to improve the upper abdominal wall contour[30]. Even scarcer are the reports of a reverse abdominoplasty as a reconstructive procedure after wide oncological resections[22, 31, 32], despite its potential and its advantages, the foremost of which are: 1.Reliable flap providing locoregional tissue with similar texture and appearance. 2. Straight forward and not time consuming dissection. 3. Contribution of considerable bulk to obliterate defects[22]. 4. It can be used in combination with other flaps[31] when there is insufficient tissue or as soft tissue coverage, eventually over a prosthetic mesh[22], for defects as big as 690 cm^2 [31] (somewhat larger than case 1 of the present report). 5. Since it requires no preoperative workup, it is also readily available in the emergency setting[22]. Furthermore its application does not preclude the use of other pedicled (e.g. lat. dorsi) or free flaps, in futurereconstruction of a defect of the same area. Although it is not advocated as a first-line choice for oncological trunk reconstruction in all cases, we agree with Pantelides et al[22] that it offers an excellent solution in complex cases where the risk of recurrence is high. Where a limited further resection is necessary, a part of the abdominoplasty is removed and the surrounding tissues are advanced. In case of a larger defect, all other reconstructive options remain open.

Patient 1 of this report is tumor free at 24 months post resection/reverse abdominoplasty and no further surgery is currently planned. She, like the four patients described by Pantelides et al[22], was a parous woman with adequate lower abdominal laxity, which enabled the mobilized abdominal flap to advance superiorly. A patient with a slim figure and a tight abdomen, however, may eventually be a contraindication to a reverse abdominoplasty, especially if the chest defect exceeds the width of 10 cm.

Chest wall resection and reconstruction can im-

prove long-term survival of patients with an extensive T4 breast cancer, primary or recurrent, if curative resection with negative surgical margins is achieved. In any case, even if the resection is of palliative nature, quality of life is significantly improved. In a retrospective study of 44 female patients from the University of Texas, M.D. Anderson Cancer Centre (curative resection n=36, palliative resection n=8), no difference was found in median survival (44.7 m vs 36.0 m, p=0.752) nor in 1-, 2-, and 3-year survival rates between primary breast cancer (78.4 %, 78.4 %, 39.2 %) and recurrent one (70.9 %, 70.9 %, 70.9 %, p< 0.05). However, both median survival (16.0 m) and the 1-, 2-, and 3-year survivalrates (30.0 %, 15%, 0) in patients with metastasis were much poorer than those in patients with primary breast cancer (p=0.003) or recurrence (p=0.018). The survival rates of patients with curative resection (36.0 m, 71.5%, 65.7 %, 65.7 %) were much longer than those with palliative resection (15.1 m, 35.1 %, 23.4 %, 7.8 %, p=0.018)[33].

In another retrospective study of 27 patients with noninflammatory, extensive locally advanced breast cancer from the European Institute of Oncology, Milan (16 with primary tumors of the breast, 11 with local recurrence after mastectomy or conservative breast surgery), two techniques were used for breast reconstruction: transverse rectus abdominis myocutaneous (TRAM) flap (n=19), and a fasciocutaneous flap (n=8). Fourteen patients (52%) died during the follow-up and the median length of survival was 16 months (range 3-79) in the TRAM flap group and 4 months (range 2-23) in the fasciocutaneous flap group. At the end of the follow-up, 10 patients were alive without evidence of disease and 3 developed metastatic disease or a local recurrence. The authors stressed the improvement in quality of life in this group of patients, with acceptable survival periods and in some cases very important survival rates[9].

If the lesion remains unresectable following systemic therapy, radiotherapy (RT) may be utilized for tumor shrinkage prior to surgery or as a definitive, palliative mode of treatment. Yee et al[2] reviewed 43 cases (24 with metastatic disease at presentation, 19 without) treated with RT. Tumor shrinkage occurred within 3 months of completing RT in 36 cases (84%). Ulceration and bleeding improved in 13 (54%) of the 24 applicable cases following RT. Median locoregional- progression-free survival for all patients was 12 months from completion of radiotherapy. Locoregional progression- free survival (p=0.2) and overall survival (p=0.4) were not significantly different between patients with and without distant metastases at presentation[2]. Similar results were noticed by other authors who reported isolated case reports of patients with unresectable breast cancers who received palliative RT [3, 34].

Patients with advanced cancers, who cannot be treated with surgery or radiotherapy, have a life expectancy averaging 6 to 12 months[35] (patient 3 of the present report). Their wounds, however, have a serious impact on the quality of life (QoL). The cross-sectional multi-center study of Lo et al[35] showed that these patients have the lowest QoL. Age, malodor, pain and psychological issues explain 87 % of total variance in quality of life[36]. Correct assessment and wound management are necessary, in order to challenge pain, malodor, bleeding etc. andimprove the QoL.Affected patients and their professional and family care givers rate pain, infection and odor management among the most important challenges in minimizing distress[37].

Current recommendations for topical control of malignant wounds in patients with breast cancer are mainly based on case reports and observational studies[38]. Initial cleansing of the wound with either sterile saline or water followed by a variety of wound dressings based on specific wound characteristics (calcium alginate, hydro cellular interface, active charcoal, and super absorbent dressings) has been utilized by most authors[7]. Exudate and bleeding is generally controlled with hemostatic dressings, calcium alginate dressings or absorbent pads[7]. Odor seems to be reduced, or even

eradicated with topical use of metronidazole (1 % solution or 0.75 % /0.80 % gel). The latter also results in improvement of wound appearance, decrease in surrounding cellulitis, halting of tissue necrosis, and decrease of pain[39].

Though a recently updated Cochrane review reminds us that evidence remains insufficient for firm conclusions supporting management of malignant wounds, it does cite two recent randomized controlled trials (RCTs), that can serve as 'current best evidence' to inform clinical decisions for alleviating some aspects of the patients' distress[37]. Lund-Nielsen et al[40] conducted a RCT to determine the influence of honey-coated compared to silver-coated bandages on treatment of malignant wounds. Improvement was observed in 62 % of participants with respect to wound size and in 58 % with respect to cleanliness. The VAS sore for malodor (p=0.007) and exudation (p<0.0001) improved significantly post intervention. Patients with reducedwound size had a median survival time of 387 days compared with 134 days in patients with no wound reduction (p=0.003). No differences were found between the two regimens[40]. The second study investigated the effectiveness of foam dressings with silver vs. foam dressings without silver to reduce malodorous and septic phenomena in malignant fungating wounds. Those dressed with foam dressings with silver showed a significant reduction of the odor compared to the ones without (p=0.049)[41]. In a more recent study, Villela-Castro et al[42] compared the effects of 0.8 % metronidazole vs. 0.2 % polyhexamethylene biguanide (PHMB) on malignant wound odor, health related quality of life, and pain, upon application. Twenty patients (83.3 %) were classified as having ' no wound odor ' at 4 days, and 100 % achieved no wound odor by day 8 (p<0.001). No difference in odor elimination or quality of life was noticed when patients managed with metronidazole were compared to those managed with PHMB. There were no statistically significant differences over time in pain measurement between the two groups[42].

Several studies have suggested that bacteria present in these wounds maybe re- sponsible for odors[43]. Proteus mirabilis and fusobacterium necrophorum seem to produce the strongest and most typical malignant wound odor[43]. The latter has been reported to be significantly greater in patients with > 105/g bacterial counts, and/or with one or more anaerobic bacteria[7]. All methods and materials currently used aim at reducing, or even eliminating, the bacterial burden; however, none has proven significantly superior to others.More clinical research to assess the comparative efficacy of different care approaches on controlling the local symptoms of these wounds is warranted. Until more substantial evidence is produced, the aforementioned methods, including our own regimen (see patient 2), adjusted to the individual patient's needs can alleviate symptoms and improve QoL in the majority of these patients.

Pain relief is another major issue for patients with extensive T4 breast cancer. Conflicting results have been reported for fungating malignant wounds. Langemo et al[44] reported pain reduction after wound care, whereas pain ratings did not change over the 42-day observation period despite thorough cleansing and wound treatment in a study from the Institute Curie, Paris[7]. Disappointing results regarding pain relief were also reported by Maida et al[6]. Tumor growths which involve bone, like case 3 of the present study, however, require a different approach, as local wound care is ineffective and meaningless. Standard treatment for such patients includes chemo/immunotherapy, radiotherapy and systemic analgesics. Radiotherapy is the treatment of choice for painful bone metastases, nonetheless 20-30 % of patients either do not respond to the treatment or present recurrent pain after treatment completion (case no 3). The latter are not suitable for further irradiation due to dose limits in normal tissues[45]. The use of conventional analgesics and adjuvants according to the principles of

the World Health Organization (WHO) analgesic ladder for cancer pain relief (1-Paracetamol and/or NSAIDs; 2-Opioids e.g. Codeine; 3-Opioids e.g. morphine, oxycodone; 4- Neurolytic blocks, spinally administered opioids), manages pain in 80 % to 90% of cancer patients[46]. Patients with side effects may benefit from interventional pain techniques, which range from simple (temporary) nerve blocks (intercostal nerves-patient 3 of this study) to more invasive techniques such as regional or neurolytic blocks or even neurosurgical procedures[47]. In recent years, there is more interest in the use of local anesthetic infusions to block peripheral nerves. Long acting local anesthetics (e.g. bupivacaine, rapivacaine) are used. Clinically relevant side effects are usually not seen at bupivacaine doses of less than 15 mg per day[47]. Nerve blocks are easier to perform, due to more efficient identification of the nerve, and achieve better analgesic outcomes[47]. Addition of dexamethasone to the local anesthetic seems to prolong block duration, reduce the worst pain and reduce opioid use[48]. A ceiling effect with a perineural dexamethasone dose of 4 mg when combined with short-/intermediate-acting or long-acting local analgesics was found in a recent metaanalysis[49].

Conclusion

Prevalence of malignant fungating wounds seems to be lower than previously; however, 5-10 % of tumors, particularly in breast cancer, are expected to fungate. These, together with the remaining extensive T4 breast tumors pose great problems to the patients and great challenges to the medical staff, regardless of the therapeutic or palliative intent of their management. The paucity of scientifically sound trials leads clinicians to act empirically and on an individual patient's needs basis. The necessity for well-designed and executed RCTs is obvious. Until then, thorough knowledge of the problems and the currently available solutions is mandatory by all breast teams, in order to at least improve the QoL of these patients.

Conflict of interest

There is no conflict of interest to declare.

Informed consent

Informed consent was obtained.

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