Radiation-associated angiosarcoma after breast cancer: Improved survival by excision of all irradiated skin and soft tissue of the thoracic wall? A report of six patients

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To the Editor,

Breast conserving treatment (BCT) with radiotherapy has replaced mastectomy as the standard care for early stage breast cancer in the last few decades. A rare and severe treatment complication is the occurrence of secondary angiosarcoma which has been associated to radiotherapy and lymphedema after a median latency period of 4–8 years [1–4]. Even though the absolute risk of secondary angiosarcoma after radiotherapy for breast cancer is estimated to be $<0.5\%$, improved breast cancer survival rates imply that an increasing number of individuals are at risk of this side effect.

Angiosarcomas are highly invasive tumors and grow in a multifocal pattern; the risk of local recurrence and metastasis after surgery is high [1,5,6]. The effect of adjuvant systemic treatment is unclear although recent studies of targeted therapies have shown promising results [7]. Earlier case series have reported better tumor control with aggressive surgical approaches [5,8], but the extent of the resection needed is neither determined nor described in detail. Here, we present long-term survival in six patients with secondary angiosarcoma after breast cancer treated with resection of all irradiated skin and associated extra thoracic soft tissue.

Six women with localized secondary angiosarcoma of the thoracic wall after breast cancer treatment were included in this series, all treated at our Sarcoma Center in Lund, Sweden. The patients were diagnosed with breast cancer between ages 42 and 67, treated with BCT and adjuvant radiotherapy with 60 Gy over 25 fractions. Two patients also received post-operative chemotherapy (six cycles of CMF or FEC, respectively). The latency time to secondary angiosarcoma was 5–9 years (Supplementary Table I to be found online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2014.983657).

The surgical treatment of the secondary angiosarcoma was planned for inclusion of all irradiated skin

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using radiotherapy coordination tattoos and the patient's radiation dose planning charts (Figure 1a). Pre-operative magnetic resonance imaging (MRI) was used to determine the resection depth needed to achieve wide surgical margins in relation to the thoracic wall. The latter varied from including the deep fascia and superficial muscle tissue to include all extra thoracic muscles and sometimes periosteal stripping of the ribs. Reconstructions were performed using pedicled m. latissimus dorsi or m. rectus abdominis flaps, and split thickness skin grafts (Figure 1b–d). The resected area was 15–20 cm by 25–30 cm. All wounds healed with the primary reconstructions. In one patient complementary cosmetic reconstructive surgery was performed.

Four patients were treated with resection of all irradiated tissue for the first presentation of secondary angiosarcoma and three of them had no local or distant tumor recurrence and were alive without evidence of disease at latest follow-up (FU) at 1.8, 6 and 6.5 years, respectively (Figure 2). The fourth patient was diagnosed with pulmonary metastases one month after surgery and died six months later.

For two patients, the initial treatment with local resection was performed in other hospitals and they were treated with resection of all irradiated tissue due to local recurrence. Both had further recurrences after the resection of all irradiated tissue. In the first case, the patient developed a metastasis in the contralateral axillary lymph nodes nine months after surgery. The lymph node metastasis was resected and the area treated with radiotherapy (50 Gy over 25 fractions). At latest FU the patient was disease-free at 5.5 years. The second patient developed a local recurrence after 2.5 years. The tumor was excised with wide margins and the patient treated with adjuvant radiotherapy (50 Gy over 25 fractions). At latest FU, she was disease-free at seven years.

The main treatment of radiation-associated secondary angiosarcoma after breast cancer treatment is surgery. The effect of adjuvant systemic treatment is unclear [7]. Despite free surgical margins, the prognosis is dismal with five years survival rates of 30–50% [5,9–11]. Using more aggressive surgical approaches, earlier center-based case series have shown that long-term survival is possible to achieve [4,5,8,11–14]. However, few studies have defined the extent of surgical margins needed and only rarely is the median size of the excision reported [5,14]. Most studies describe that the operations were performed as mastectomies or as wide excisions (when the patient had undergone mastectomy as part of the previous breast cancer treatment).

Here we present a small case series with long-term survival in five of six patients treated with an extensive

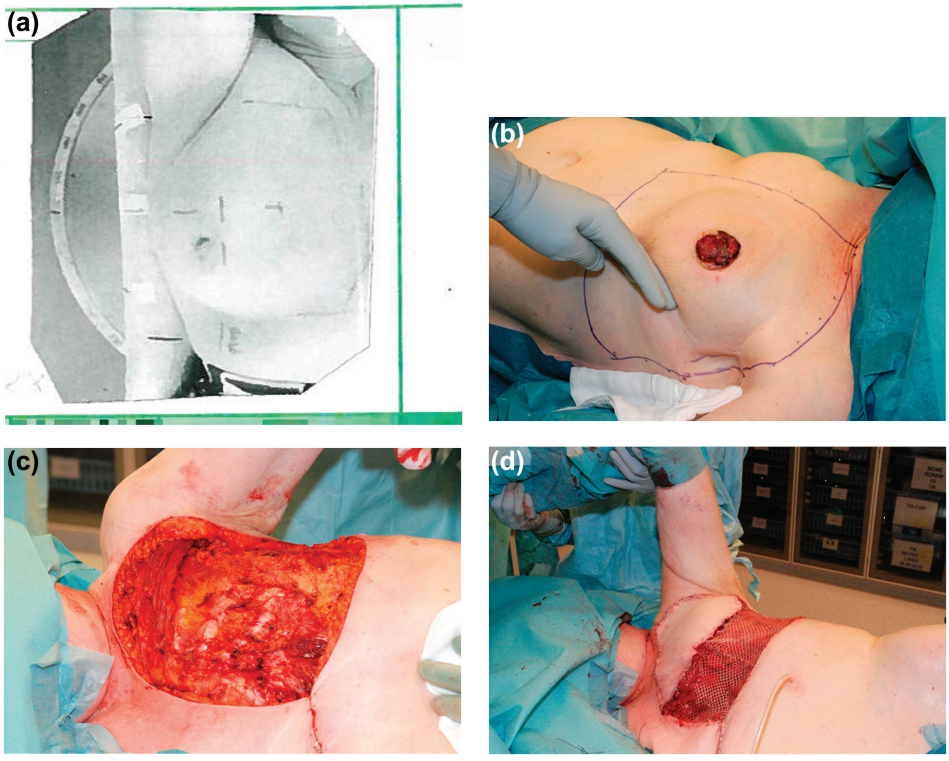

Figure 1a–d. Using the radiotherapy dose planning charts the resection area is planned, patient 3 (a). The irradiated area is marked to define the extent of the resection (b). The skin and extra thoracic soft tissue is resected (c) and a pedicled flap of the latissimus dorsi and a split-thickness skin graft is used for reconstruction (d), patient 6 (b–d).

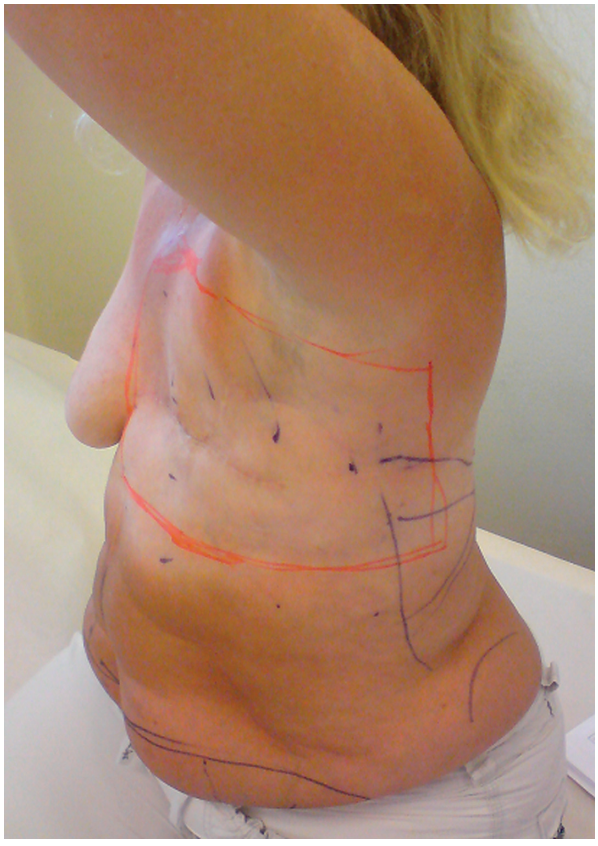

Figure 2. Patient 1, 1 year after surgery.

surgical approach for secondary angiosarcoma. All irradiated skin and subcutaneous tissue, determined according to radiotherapy coordination tattoos and dose planning charts, was excised. Deep surgical margins were planned in relation the extension of tumor as evaluated by MRI, and had to include all extra thoracic muscle tissue in some cases. Despite recurrences in two patients, long-term survival appears to have been achieved. Although our series is small it presents a treatment strategy for secondary angiosarcomas after breast cancer treatment. The outcome suggests that this aggressive surgical approach is motivated and that aggressive treatment of solitary tumor recurrences also should be considered.

We recommend that patients with suspected secondary angiosarcoma after breast cancer treatment are referred to a multidisciplinary sarcoma center for evaluation, diagnosis and treatment.

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Supplementary material available online

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