Case Report

Prolonged Large Seroma Formation after Breast-Conserving Therapy

Shuhei Suzuki  Shoji Oura  Shinichiro Makimoto

Department of Surgery, Kishiwada Tokushukai Hospital, Kishiwada-city, Japan

Keywords
Breast cancer · Capsulectomy · Long-lasting seroma · Radiotherapy

Abstract
A 78-year-old obese woman with breast cancer underwent breast-conserving surgery and axillary lymph node dissection. Due to the prior exposure to long-term taxan chemotherapy for her recurrent gastric cancer, the patient did not undergo adjuvant chemotherapy and began to receive radiotherapy to both the conserved breast and supraclavicular region on the 39th day after operation. Two aspiration therapies were done to the enlarging seroma only at the initial phase of the radiotherapy. No further aspiration therapies were done to the seroma during and after radiotherapy for more than 3 months despite the undoubtable seroma formation. High degree of tension due to large seroma formation, extended from the axilla to deep into the breast parenchyma, made the patient request us to heal the long-lasting seroma. Five aspiration therapies and one simultaneous minocycline intrathecal injection therapy did not bring about wound healing. To heal the persistent seroma, capsulectomy was done to the encapsulated lesion 7 months after the operation. Resected capsule was 110 × 45 mm in size and had smooth inner surface. Pathological study showed the seroma capsule mainly consisting of fibrous tissue with some inflammatory changes. Postoperative course was uneventful, and wound healing was promptly obtained after capsulectomy. Breast surgeons and radiation oncologists should note this type of unfavorable radiation-induced adverse event after breast-conserving therapy.

Introduction
Breast-conserving therapy has greatly contributed to the well-being of breast cancer patients. Breast-conserving therapy consists of partial resection of the affected breast and postoperative adjuvant radiotherapy to the conserved breast. It is well known that postoperative
Radiotherapy can reduce in-breast recurrence to a third compared to that of partial mastectomy alone. Therefore, breast cancer patients except for older patients with positive estrogen receptor and negative surgical margins should receive radiotherapy to the conserved breast of its beginning within 20 weeks [1] after breast-conserving surgery.

Adjuvant radiotherapy to the conserved breast can contribute to the local control on the one hand but cause long-term and short-term toxicities on the other hand. The former includes cardiotoxicity, lung injury, and second malignancies. The latter includes arm edema, skin fibrosis, pneumonitis, and inhibition of wound healing.

Breast-conserving surgery, i.e., main treatment for operable early breast cancer, also can cause seroma formation [2] and breast infection [3]. The former is much often observed compared to the latter in daily clinical practice and generally needs at least one or two aspiration therapies to the enlarging seroma. This complication is more often clinically observed in obese patients than in average or lean patients [4]. We herein report a rare case of prolonged large seroma formation after breast-conserving therapy.

**Case Report**

A 78-year-old obese, i.e., body mass index of 28.8, woman with a luminal type breast cancer in her left upper and outer quadrant of the breast underwent breast-conserving surgery and axillary dissection in February 2020. The patient had developed liver hilus node recurrence from gastric cancer approximately 8 years before and had been heavily treated with the second-line paclitaxel chemotherapy for more than 5 years in addition to the short-term first-line cisplatin-containing chemotherapy. She fortunately got a presumed cure of the gastric cancer recurrence but suffered from severe and irreversible peripheral neuropathy with the paclitaxel chemotherapy. The patient, therefore, began to receive adjuvant endocrine therapy using aromatase inhibitor without chemotherapy despite the confirmation of massive lymph node metastases after breast cancer surgery. The patient also began to receive radiotherapy to both the conserved breast and supraclavicular region on the 39th postoperative day. The patient received aspiration therapy for the enlarging seroma two times at the beginning of radiotherapy but did not receive aspiration therapy thereafter as directed by the radiation oncologist even though undoubtable seroma formation was observed. The patient unfortunately began to develop etiology-unknown diarrhea just after the completion of radiotherapy and was hospitalized to alleviate the abdominal symptom for a month. After discharge from the hospital with some symptom relief, i.e., at more than 3 months from the completion of radiotherapy, strong local tension due to large seroma formation made the patient request us to heal the long-lasting seroma (Fig. 1). Ultrasound showed massive and persistent fluid retention and presumed capsule formation just around the seroma. Computed tomography showed a large seroma extending from the axilla to deep into the conserved breast.

**Fig. 1.** Skin protrusion due to large seroma formation. Marked skin protrusion (arrows) was observed in the upper and outer quadrant of the left breast.
parenchyma with presumed capsule formation (Fig. 2). Five aspiration therapies did not lead
to wound healing. Simultaneous minocycline, i.e., 100 mg diluted in 20 mL saline, intrathecal
injection once into the seroma cavity did not cause tissue adhesion either. To heal the
persistent seroma, capsulectomy under general anesthesia was planned 7 months after the
operation. In the operation, almost all the capsule except for the part of presumed
attachment to the axillary vein was surgically resected. The resected capsule was 110 × 45 mm in size and
had smooth inner surface (Fig. 3a, b). Pathological study showed a seroma capsule consisting
of fibrous connective tissue with hyalinization, no epithelial cells, and mild precipitation of
fibrin on the surface of pseudocystic wall. In the superficial layer of the pseudocystic wall,
aggregation of foamy histiocytes, infiltration of lymphocytes, and growth of capillary blood vessels were observed (Fig. 3c, d). The patient recovered uneventfully, was discharged on the 8th postoperative day, and thereafter showed prompt wound healing.

**Discussion**

After applying primary breast-conserving surgery for breast cancer patients with massive lymph node metastases, adjuvant chemotherapy generally precedes both radiotherapy and endocrine therapy [5]. More than ten lymph node metastases in this case, therefore, should have made the patient receive intensive adjuvant chemotherapy, e.g., dose-dense chemotherapy [6]. This patient, however, had already received more than 5 years' weekly paclitaxel chemotherapy, resulting in irreversible peripheral neuropathy and extremely rare long-lasting clinical complete response of the lymph node recurrence from gastric cancer in the liver hilum. This patient, therefore, seemed unlikely to benefit from adjuvant taxan chemotherapy with the intent to reduce the recurrence rate of breast cancer. Anthracycline-containing chemotherapy was also judged to have little or, even if present, nominal benefit to the patient as a postoperative adjuvant chemotherapy when considering the patient's age of 78 years old [7]. The patient, therefore, started to receive adjuvant endocrine therapy without chemotherapy.

Fibrous capsule is generally formed just around the silicone implant, and capsular contracture often aggravates the cosmetic outcome of the patients after silicone-based breast reconstruction [8, 9]. In addition, after capsule formation, simple silicone removal due to either infection or silicon damage generally leads to persistent seroma formation in the capsule and never results in wound healing unless at least major part of the capsule is removed. It, therefore, is very important to avoid capsule formation after breast cancer surgeries. Possible measures to prevent seroma formation include postoperative full lymph drainage, appropriate aspiration of enlarging seroma followed by compression of the seroma cavity with some kind of girdle, and intrathecal injection of some chemical irritants such as minocycline and picibanil into the seroma cavity.

Local control and survival rates are lower if postoperative irradiation begins later than 20 weeks after surgery [1]. In this case, the patient began to receive adjuvant radiotherapy about 6 weeks after surgery. The timing of starting radiotherapy itself seemed to be common and reasonable, but we lacked the discreetness, probably due to the massive lymph node involvement, to start radiotherapy after making a proper judgment about wound healing. In addition, radiation oncologist's concern that aspiration therapy to the enlarging seroma could affect the efficacy and side effects of radiotherapy also had a major impact on the persistent large seroma formation in this case.

We had reported a case of massive seroma formation after breast cancer surgery successfully treated with intrathecal minocycline injection [10]. In this case, we also did the intrathecal minocycline injection into the seroma cavity once, only leading to minor histological findings of mild precipitation of fibrin on the surface of pseudocystic wall and no adhesion of the pseudocystic walls.

To the best of our knowledge, this is the first case of prolonged large seroma formation extending from the axilla to deep into the breast parenchyma encompassed by fibrous capsule without silicone-based breast reconstruction. It is well known that some kind of solid foreign body is generally separated by fibrous capsule, resulting in spherical transformation in order to minimize the contact area between the human body and the foreign body when the foreign body being deformable. To date, there should have been quite a few cases in which radiation therapy was started without complete healing of the wound in clinical practice. Why this
persistent large seroma occurred in this patient remains unclear. But breast surgeons and radiation oncologists should note this minor but clinically important adverse event after breast-conserving therapy. In conclusion, breast surgeons should pay much attention to the postoperative persistent seroma formation to avoid the aggravation of quality of life of the breast cancer patients.

**Statement of Ethics**

The study was approved by the Kishiwada Tokushukai Hospital Ethics Committee (IRB #Case 20-04). Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

**Funding Sources**

No funding was received for this research.

**Author Contributions**

Suzuki S. contributed to the design of the report. Oura S. drafted the manuscript. Makimoto S. revised the manuscript. All authors have read and approved the final version of the manuscript.

**Data Availability Statement**

All data generated during this study are included in this article. Further inquiries can be directed to the corresponding author.

**References**

1. Olivetti IA, Lesperance ML, Truong PT, Nichol A, Berrang T, Tyldesley S, et al. Intervals longer than 20 weeks from breast-conserving surgery to radiation therapy are associated with inferior outcome for women with early-stage breast cancer who are not receiving chemotherapy. *J Clin Oncol.* 2009;27:16–23.
2. Boostrom SY, Throckmorton AD, Boughey JC, Hallfield AG, Zakaria S, Hoskin TL, et al. Incidence of clinically significant seroma after breast and axillary surgery. *J Am Coll Surg.* 2009;208:148–50.
3. Brewer VH, Hahn KA, Rohrbach BW, Bell JL, Baddour LM. Risk factor analysis for breast cellulitis complicating breast conservation therapy. *Clin Infect Dis.* 2000;31:654–9.
4. Pogson CJ, Adwani A, Ebbs SR. Seroma following breast cancer surgery. *Eur J Surg Oncol.* 2003;29:711–7.
5. Balduzzi A, Leonardi MC, Cardillo A, Orecchia R, Delpasqua S, Iorfida M, et al. Timing of adjuvant systemic therapy and radiotherapy after breast-conserving surgery and mastectomy. *Cancer Treat Rev.* 2010;36:443–50.
6. Lemos Duarte I, da Silveira Nogueira Lima JP, Passos Lima CS, Delee Sasse A. Dose-dense chemotherapy versus conventional chemotherapy for early breast cancer: a systematic review with meta-analysis. *Breast.* 2012;21:343–9.
7 Early Breast Cancer Trialists’ Collaborative Group. Adjuvant chemotherapy in oestrogen-receptor-poor breast cancer: patient-level meta-analysis of randomised trials. Lancet. 2008;371:29–40.
8 Araco A, Caruso R, Araco F, Overton J, Gravante G. Capsular contractures: a systematic review. Plast Reconstr Surg. 2009;124:1808–19.
9 Schaub TA, Ahmad J, Rohrich RJ. Capsular contracture with breast implants in the cosmetic patient: saline versus silicone – a systematic review of the literature. Plast Reconstr Surg. 2010;126:2140–9.
10 Tanaka K, Oura S, Yasuda K, Makimoto S. Abrupt aggravation of encapsulated seroma after breast reconstruction with extended latissimus dorsi muscle flap. Case Rep Oncol. 2021;14:290–5.