Surgical Treatment for Solitary Recurrence of Breast Cancer to the Internal Mammary Lymph Nodes : Report of Three Cases

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Abstract

Three cases with solitary recurrence of breast cancer to the internal mammary lymph nodes (IMNS) with no other distant recurrences after radical operation are described herein. The first case involved a 51-year-old Japanese woman who had undergone treatment 8 years earlier for pT1pN0M0, with recurrence developing in the IMNs 2 years later. Six years after the IMNs relapse, IMNs were dissected and two of 5 IMNs were positive for carcinoma. The second case involved a 43-year-old Japanese woman in whom recurrence of IMN was detected on ultrasonography (US), computed tomography (CT) and positron emission tomography 13 months after the primary operation for pT2pN1M0. One of 20 dissected lymph nodes was positive for carcinoma. Sentinel lymph nodes (SNs) visualized by lymphoscintigraphy were detected in the internal mammary region and axilla at the time of primary operation, but IMNs were left and followed up postoperatively rather than dissected. A third case involved a 55-year-old Japanese woman in whom solitary recurrence of IMN was detected by US, CT and cytological examination 13 months after primary operation for pT2pN0M0. One of 4 dissected lymph nodes was positive for carcinoma.

Introduction

As support increases for the sentinel lymph node (SN) concept, management of the internal mammary lymph nodes (IMNs) at initial treatment of breast cancer is increasingly being seen as important. Solitary tumor recurrence in IMNs after radical operations in patients with breast cancer is not uncommon, but surgical treatment is not generally recommended, as IMNs are treated as an area distant from the breast. We dissected recurrent IMN lesions that were detected as solitary recurrences within three years after initial radical operations in 3 patients with breast cancer. Informed consent was obtained preoperatively from these patients.

Case Reports

Case 1

A 51-year-old Japanese woman with a mass lesion in the upper lateral area of the right breast underwent modified mastectomy for radical treatment of breast cancer in October 1991 at another hospital. Histological examination identified a 15×12 mm invasive ductal carcinoma, Scirrhous carcinoma, and axillary lymph

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Abbreviations: internal mammary lymph node (IMN), sentinel lymph node (SN), estrogen receptor (ER), computed tomography (CT), ultrasonography (US), positron emission tomography (PET)

nodes were negative for metastasis (0/11). Estrogen receptor (ER) status was negative and progesterone receptor (PgR) status was not evaluated. Twenty-nine months postoperatively, blood serum CEA levels were elevated and computed tomography (CT) and ultrasonography (US) revealed enlargement of the internal mammary lymph node at the level of the 2nd intercostal space (ICS). Serum CEA levels normalized in response to radiotherapy and chemotherapy with cyclophosphamide (100 mg/body), methotrexate (40 mg/m^2) and 5-fluorouracil (500 mg/m^2) twice monthly for 6 courses,

but response periods soon became shorter (Fig.1). CT and bone scintigraphy revealed no other distant metastasis. In October 1999, 8 years after the first operation, IMNs at the level of the 2nd ICS were dissected via an extra-pleural approach. Histopathological examination identified metastases of the breast cancer in 2 of the 5 nodes. Serum CEA levels normalized postoperatively and no elevation has occurred for 5 years.

Case 2

A 43-year-old Japanese woman with a 30 mm upper-

Table 1. Clinical findings of the IMN recurrent cases.

Case	Age (years)	Operation	TNM Classification stage	No. of axillary Metastases /resection	adjuvant therapy	Disease free survival (months)	Location of the recurrence Intercostalis level	No. of recurrent IMN /resection	Survival after the IMN dissedtion (months)
1	51	Bt+Ax	pT1pN0M0 stageI	0 / 11	none	29	2nd	2 / 5	61 alive
2	43	Bq+Ax	pT2pN1M0 stageIIB	1 / 20	chemotherapy*	13	1st	1 / 16	24 alive
3	54	Bt+Ax+Ic	pT2pN0M0 stageII A	0 / 17	chemotherapy*	13	2nd	1 / 3	17 alive

*: cycrohosphamide (100 mg) and 5'DFUR (600 mg).

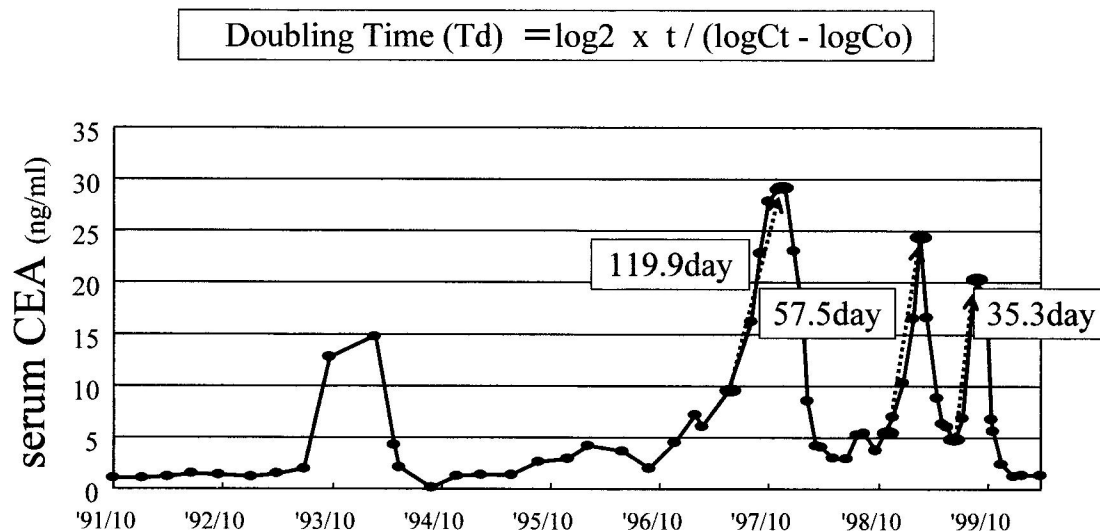$$\text{Doubling Time (Td)} = \log 2 \times t / (\log Ct - \log Co)$$

Fig. 1. Serum CEA level of Case 1 after the primary operation. Serum CEA levels normalized in response to radiotherapy (April 1994) and systemic chemotherapy (February 1998, March 1999), but both of response periods and doubling time of the serum CEA soon became shorter.

inner quadrant mass in the left breast underwent excisional biopsy for diagnosis in November 2001 at another hospital. After a histological diagnosis of invasive ductal carcinoma, papillotubular carcinoma, with lymphatic vessel permeation was confirmed, the patient was referred to our hospital. We suspected residual cancer of the breast without axillary metastasis. To detect SNs and execute lymphatic mapping, a total of 4.2 mCi of technetium 99m tin colloid was injected as a radiocolloid in 0.5mL quantities into 3 sites around the operation scar. Lymphoscintigraphy obtained 2 h after injection enabled

visualization of 2 hot nodes as SNs in both the axilla and internal mammary region (Fig.2). Breast-conserving therapy and axillary lymph node dissection were performed as a radical operation in December 2001. Histopathological examination revealed 1 metastatic lymph node out of 20 resected left axillary lymph nodes. The main tumor of the left breast was negative for both ER and PgR, and negative for HER2. Postoperative adjuvant chemotherapy was added, with cyclophosphamide (100 mg/day) and 5' DFUR (600 mg/day).

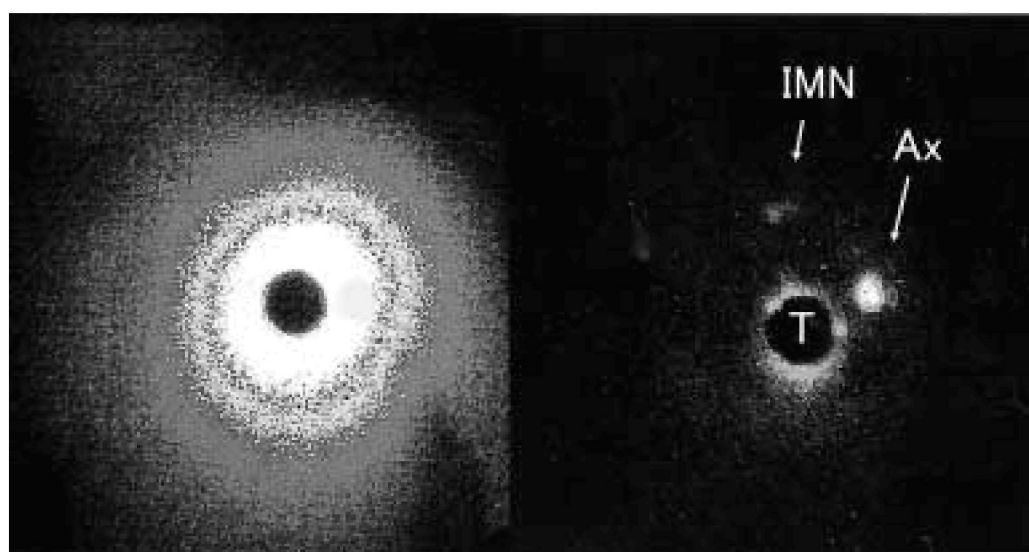In November 2002, CT and US revealed a swollen

Fig. 2. Two sentinel lymph nodes detected in the internal mammary region and axilla by lymphoscintigraphy at the time of primary operation (Case 2).
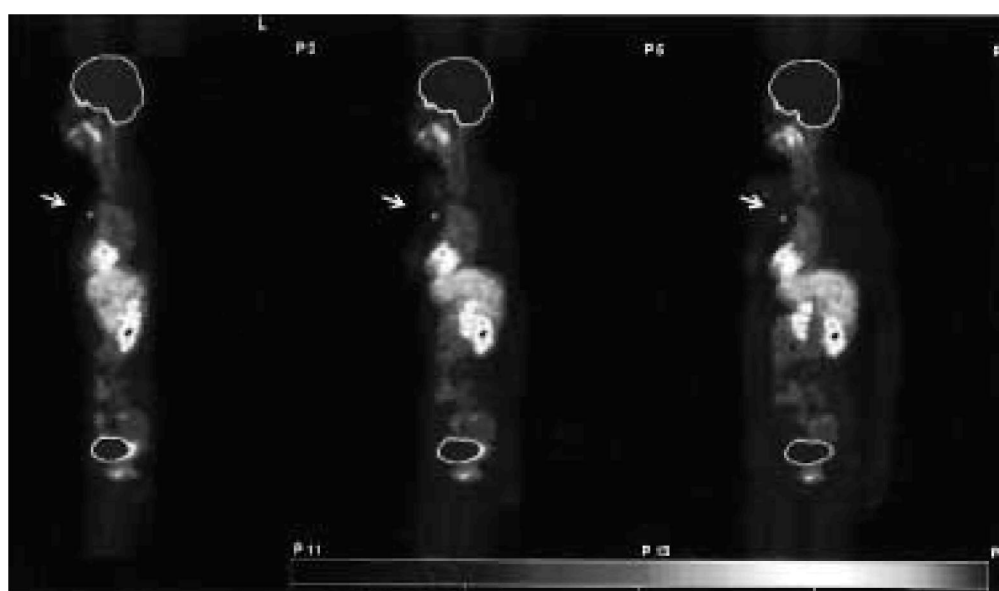

Fig. 3. Internal mammary lesion was detected as a positive signal (allow) by PET (Case 2).

IMN at the level of the 1st ICS, showing as a positive signal on positron emission tomography (PET) (Fig.3). CT and bone scintigraphy revealed no other distant metastasis. In January 2003, IMNs from the level of the 1st to 3rd ICS were dissected via an extra-pleural approach. Histopathological examination revealed breast cancer metastasis in 1 of the 16 resected nodes. Adjuvant chemotherapy with cyclophosphamide (100 mg/body), methotrexate (40 mg/m^2) and 5-fluorouracil (500 mg/m^2) was added twice a month for 6 courses. The patient has remained disease-free for 2 years since the second operation.

Case 3

A 54-year-old Japanese woman with a 45-mm inner-upper quadrant mass in the left breast diagnosed as T2N0M0 Stage II underwent a modified radical mastectomy in June 2002. To detect SNs and perform lymphatic mapping, a total of 3.5 mCi of technetium 99m tin colloid was injected as radiocolloid in 0.5 mL quantities into 3 sites around the tumor. Lymphoscintigraphy revealed 1 hot node in the axilla as a SN. Histological diagnosis was invasive ductal carcinoma, Solid-tubular carcinoma, with lymphatic vessel permeation and no metastasis identified in 17 resected axillary nodes. The main tumor of the left breast was negative for ER, PgR and HER2. Postoperative adjuvant chemotherapy was added using cyclophosphamide (100 mg/day) and 5' DFUR (600 mg/day).

In June 2003, CT and US revealed swelling of an IMN at the level of the 2nd ICS (Fig.4). Fine needle aspiration biopsy of the lesion revealed adenocarcinoma cells. PET detected no positive lesions and CT and bone scintigraphy revealed no other distant metastasis. IMNs from the level of the 1st to 3rd ICS were dissected via an extra-pleural approach. Histopathological examination revealed breast cancer metastasis in 1 of 4 nodes. Adjuvant chemotherapy with Paclitaxele (80 mg/m^2) was added weekly, 3 times a month for 4 courses. The patient has remained disease-free for 17 months since the second operation.

Discussion

The 3 cases described herein demonstrate that solitary metastases to IMNs after curative operations for breast cancer can represent valid targets for surgical intervention. Particularly in processes to detect SNs, traces to the IMNs on lymphoscintigraphy can identify primary recurrent lesions within a short period after radical operations for breast cancer.

Metastases to IMNs are quite frequent, occurring in 17-30% of selective patients with larger and more centrally/medially located tumors who were performed
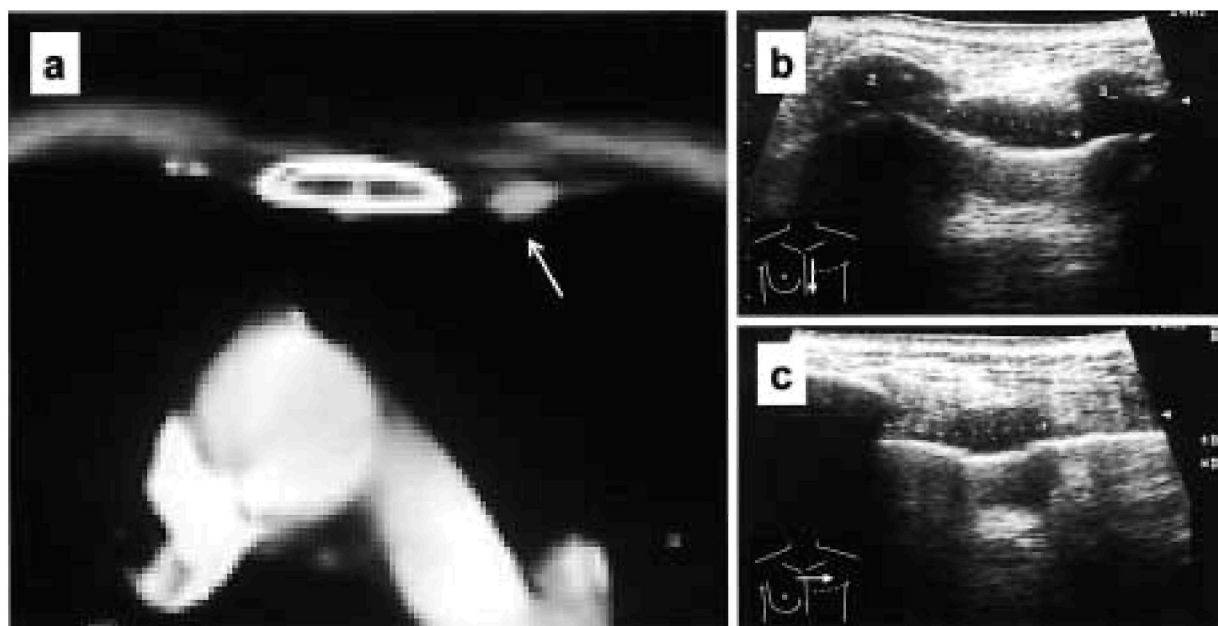

Fig. 4. Internal mammary node was detected by CT (a) and US (b: sagital scan, c: transverse scan) on the 2nd intercosal space (Case 3).

extended radical mastectomy in '60 and '70[1]. Veronesi et al. reported that patients with positive axillary nodes showed metastasis to IMNs in 29.1% of cases, while isolated internal metastases appeared in 9.1% of patients with axillary negative nodes[2]. Lacour et al. compared to radical mastectomy and extended mastectomy and concluded that dissection of the IMNs significantly decreases the risk of death for patients with internal tumors and positive axillary nodes but extended mastectomy conversely seemed to increase risk of death for patients with external tumors and negative axillary nodes[3]. Information on the presence or absence of IMN metastasis would be of great importance in determining prognosis for breast cancer patients[2], so radical resection of IMNs at the time of mastectomy is uncommon.

Cody et al.[1] reported the results of a multivariate analysis showing that IMN status was second only to axillary lymph node status in predicting disease-free survival after the 10-year follow-up. The 10-year disease-free survival rate was 72.8% in patients without node metastases, 47.2% in patients with axillary node metastases only, 51.9% in patients with IMN metastases only, and 24.9% in patients with involvement of both groups of nodes[2]. In addition, failure to consider IMN status in T1N0 patients may result in undertreatment of a significant proportion of stage I patients, so accurate knowledge of IMN status by biopsy of the ICSs is important [2,4].

Some patients with untreated metastatic IMNs have experienced relapse of these nodes. Compared with axillary relapse[5], these events are extremely rare[6]. Frequency of IMN recurrence in patients undergoing adjuvant therapy (CMF) is very low, at about 0.11%[7]. Asagoe et al. reported 2 cases after standard radical mastectomy and 1 case after extended radical mastectomy, with a frequency of 6% . Despite treatment with radiotherapy and other adjuvant therapy, all 3 patients died from other distant recurrence[8]. In contrast, present case 1 has remained alive without recurrence for 6 years after resection of recurrent lymph nodes. Solitary recurrence in the IMNs was considered limited to this local area.

Treatment of these relapsed nodes remains contentious[9]. Noguchi et al. reported that surgical treatment was effective in patients with long disease-free periods and no other distant metastasis[10]. Radiotherapy was also recommended due to equal effectiveness with

surgical resection[11]. Surgical or irradiative dissection could offer sufficient treatment for these patients, since patients with restricted IMN recurrence may not have a bad prognosis[12].

Internal mammary SNs are visualized in 13-21% of patients[13-15]. Haryono et al. detected IMNs as SNs by lymphoscintigraphy on primary surgical treatment and undertook resection of these nodes, leading to patient up-staging and changes in subsequent management[16]. Francisco et al. also diagnosed the involvement of IMNs with axillary-negative nodes using preoperative lymphoscintigraphy[17]. In Case 2, although IMN was detected as SN at the primary operation resulting in recurrence shortly after primary treatment, we did not perform dissection them because breast conversing surgery was selected for her upper outer lesion. It was suggested that SNs were existed not only axilla but also ICS in this case.

In conclusion, recent improvements in US, CT and PET techniques have allowed a higher rate of detection of IMN metastases. When we encounter a patient with solitary recurrence to the IMNs shortly after the primary operation, with no other distant metastasis, surgical resection of the IMNs appears to offer good results, particularly in patients with axillary-negative involvement or with IMNs detected as SNs at the time of primary operation. Also, we suggest that the time is ripe to aggressively introduce techniques for detecting SNs, not only for axilla-conserving surgery but also in the management of IMNs.

References

1) Cody HS, Urban JA. Internal mammary node status: A major prognosticator in axillary node-negative breast cancer. Ann Surg Oncol 1995; 2: 32-37.

2) Veronsei U, Cascinelli N, Greco M, Bufalino R, Morabito A, Galluzzo D et al. Prognosis of breast cancer patients after mastectomy and dissection of internal mammary nodes. Ann Surg 1985; 202: 702-707.

3) Lacour L, Le MG, Hill F, Kramar A, Contesso G, Sarrazin D. Is it useful to remove internal mammary nodes in operable breast cancer? Eur J Surg Oncol 1987; 13: 309-314.

4) Noguchi M, Kitagawa H, Kinoshita K, Eafashi M, Miyazaki I. Reappraisal of internal mammary lymph

node dissection in selected patients with invasive breast cancer. Surg Today 1994; 24: 795-802.

5) Fisher B. The revolution in breast cancer surgery: science or anecdotalosm? World J Surg 1985; 9: 655-666.

6) Veronesi U. Calagussa P. Inefficacy of internal mammary nodes dissection in breast cancer. Cancer 1981; 47: 170-175.

7) Recht BA, Pierce SM, Abner A, Vicini F, Osteen RT, Love SM et al. Regional nodal failure after conservative surgery and radiotherapy for early-stage breast carcinoma. J Clin Oncol 1991; 9: 988-996.

8) Asagoe T, Yamoto H, Hanatani Y, Nemoto A, Kurosawa T, Takada T et al. Limit of conservative surgery based on significance of extrapleural parasternal node dissection and intramammary cancer residuals after excisional biopsy for breast cancer (in Japanese with English abstract). Jpn Soc Cancer Ther 1988; 23: 2499-2506.

9) Freedman GM, Fowble BL, Nicolaou N, Sigurdson ER, Torosian MH, Boraas MC et al. Should internal mammary lymph nodes in breast cancer be a target for the radiation oncologist? Int J Radiat Oncol Phys 2000; 46: 805-814.

10) Noguchi M, Tanak S, Fujii H, Takiawa Y, Miyazaki I. The surgical management of parasternal recurrence of breast cancer. Int Surg 1985; 70: 211-214.

11) Sanger G. An aspect of internal mammary metastases from carcinoma of the breast. Ann Surg 1963; 157: 180-185.

12) Donegan WL, Spratt JS. Surgical management. In: Donegan WL, Spratt JS eds, Cancer of the breast, 4th ed. Philadelphia: Saunders 1998: 443-504.

13) Von de Ent FWC, Kenegen RAM, can der Pol HAG, Hoofwijik AGM. Eur J Surg Oncol 1999; 24: 24-29.

14) Borgstein PJ, Pijpers P, Comans EF, can Diest P, Boom RP, Meujer S. Sentinel lymph node biopsy in breast cancer: guidelines and pitfalls of lymphoscintigraphy and gamma probe detection. J Am Coll Sur 1998; 186: 275-283.

15) E. Leppanen, Leidenius M, Krogerus L, con Smitten K. The effect of patient and tumour characteristics on visualization of sentinel nodes after a single intratumoural injection of Tc 99m labeled human albumin colloid in breast cancer. Eur J Sur Oncol 2002; 28: 821-826.

16) Haryono SJ, Tanis PJ, Nieweg OE, Olmos RAV, Rutgers EJT. Isolated internal mammary sentinel lymph node metastasis in two breast cancer patients. Int J Clin Oncol 2002; 7: 368-371.

17) Julian FJ, Rfaile M, Llatjos M, Rull M, Fuste J, Castella E and et al. Internal mammary sentinel node metastases in an otherwide lymph-node negative breast cancer patient. Breast Journal 2002; 8: 317-319.

乳癌根治術後の胸骨傍リンパ節再発に対して外科治療を行った3例

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　　乳癌の根治術後に胸骨傍リンパ節（IMN）単独再発を来たし，外科的切除を行い良好な成績を得た3症例を報告する。症例1；初回手術後2年目から6年間にわたりIMNのみに病変が認められたため術後8年目に郭清術を行った。郭清術後5年経過した現在，再発徴候を認めず健存中である。長期間にわたりIMN再発部位にのみ病変が限局していた症例である。症例2；乳癌の根治術時，RI法によるセンチネルリンパ節（SN）同定（マッピング）を行い，腋窩および胸骨傍領域にhot spotが確認された。乳房温存療法および腋窩リンパ節（pN 1/20）郭清を行った13ヵ月後にIMN単独再発をきたした。郭清IMN16個中1個が転移陽性であった。IMNが腋窩リンパ節と同様にSNであったと推察される症例である。症例3；内上領域の乳癌の根治術後13ヶ月目にIMN再発が確認された。手術時にSNとして同定されたリンパ節は腋窩リンパ節のみでこれを含めて郭清したが，すべて転移陰性であった。術後13ヶ月目にIMNs郭清を行い，4個中1個が転移陽性であった。内側領域の病変ではSN以外にIMNへの転移を考慮すべきことを示唆する症例であった。いずれの症例でも，IMN再発が遠隔再発ではなく所属リンパ節としての局所再発と考えられたため，外科治療が有効であったと考えられる。