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Breast Cancer Recurrence in the Chest Wall Successfully Treated with TS-1

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Abstract : Both clinical efficacy and the quality of life (QOL) should be taken into consideration when treating elderly patients with recurrent breast cancer. The oral combined fluoropyrimidine, TS-1 (tegafur, gimeracil, and oteracil), is a novel anticancer drug. The patient was a 74-year-old female with a recurrence of invasive breast cancer in the wall of her left chest. She had undergone a radical mastectomy 27 years previously to treat left breast cancer. We diagnosed the recurrence as a triple-negative cancer by core needle biopsy and treated her with 4 courses of oral TS-1 alone, and the tumor clinically disappeared. The only adverse event observed during TS-1 therapy was Grade 2 general fatigue, but there was no decline in the patient's QOL. We therefore consider TS-1 to be a feasible antitumor agent for metastatic or recurrent breast cancer that can prevent a decrease in the QOL, thus making it especially suitable for elderly patients.

Key words : **Breast cancer, Recurrence, TS-1, Chest wall tumor, Elderly patient**

Introduction

The treatment strategy for recurrent breast cancer has long followed the approach described by Hortobagyi et al.,[1] which is to start treatment with hormone therapy if the tumor is hormone-sensitive and there are no metastases that are life-threatening, or to start with chemotherapy if the tumor is not hormone sensitive or there are life-threatening metastases. Therefore, systemic drug therapy is the main approach used for the treatment of metastatic or recurrent breast cancer, and radiotherapy or surgery are performed as a local treatment when needed. Anthracycline derivatives or taxane derivatives are regarded as the standard first-line anticancer chemotherapeutic agents for the treatment of metastatic or recurrent breast cancer, and response rates of 30% to 70% have been reported when administered as a first-line treatment.[2] However, for elderly patients, it is sometimes difficult to maintain a good quality of life (QOL) during treatment with such agents. We herein report a case in which a recurrence developed 27 years after mastectomy, in whom a long-term complete response (CR) was achieved by a treatment with an oral combined fluoropyrimidine, TS-1 (tegafur, gimeracil, and oteracil) alone.

Case Report

In August 2007, a 74-year-old female came to our institution to be examined for a left chest wall tumor. In January 2007, a mass had appeared on the wall of the anterior aspect of the patient's left chest, and it had thereafter increased in size. At the time of the initial examination, a firm, immobile, and protruding lesion with a diameter measuring 5 cm was noted in the vicinity of the surgical scar on the left anterior chest. The patient had undergone a radical mastectomy followed by radiation for the treatment of the left breast cancer 27 years prior to the detection of the recurrence. Detailed information about the previous left breast cancer, including the stage, histological type, hormone receptor status, and postoperative treatment, were unavailable. The results of the com-

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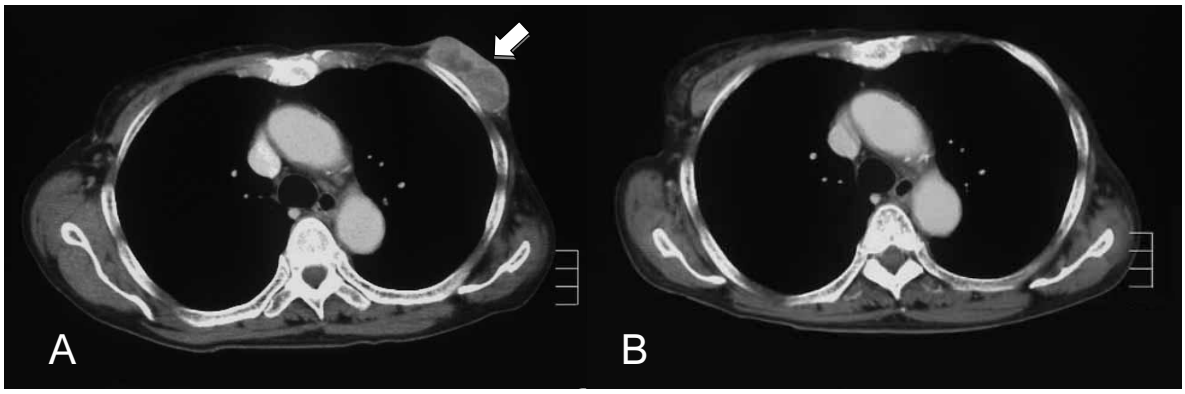

Figure 1. CT scan findings. A large tumor (arrow), was revealed on the left chest wall (A). The tumor disappeared after chemotherapy (B).

plete blood count and blood chemistry studies of the patients at the diagnosis of the recurrence were normal. Her CEA level (87.4 ng/ml) was elevated, but her CA-15-3 level (10 U/ml) was normal. Contrast CT examination of the chest showed a mass measuring 55 x 20 mm with mild contrast enhancement on the left anterior chest wall at the site of the mastectomy (Fig. 1A). The histological diagnosis was invasive ductal carcinoma of the breast (solid tubular carcinoma) by a core needle biopsy. An immunohistochemical studies revealed that the tumor subtype was triple-negative (ER 0%, PgR 0%, HER2 0) (Fig. 2). A total body examination revealed no evidence of distant metastasis, and we made a diagnosis of local recurrence in the left anterior chest wall.

Because she was 74 years old and did not want to receive standard chemotherapy due to the adverse side effects, oral TS-1 chemotherapy (100 mg/body for 28 consecutive days followed by a 14-day rest period) was started on August, 2007. At the end of the first course the mass had shrunk to the size of the tip of a little finger, and a decrease in tumor markers was also noted (CEA 87.4→36.7). Because the patient experienced general fatigue and a loss of appetite (both Grade 2), the second course of treatment was continued at a lower dose (100→80 mg/body for 14 days followed by a 7 day rest period). After the completion of 4 courses, the mass was no longer palpable and a CT examination also showed no mass (Fig. 1B). The CEA level had also decreased to within the normal range (Fig. 3). The patient wished to discontinue the TS-1 therapy at this point, the decision was made to observe her progress through follow-up.

A PET-CT examination in April of 2008 revealed accumulation in the cervical lymph nodes, and the patient was diagnosed with lymph node recurrence. After radiotherapy (60 Gy), a CT examination in September showed that the swollen lymph nodes had disappeared. No evidence of recurrence has been detected since then.

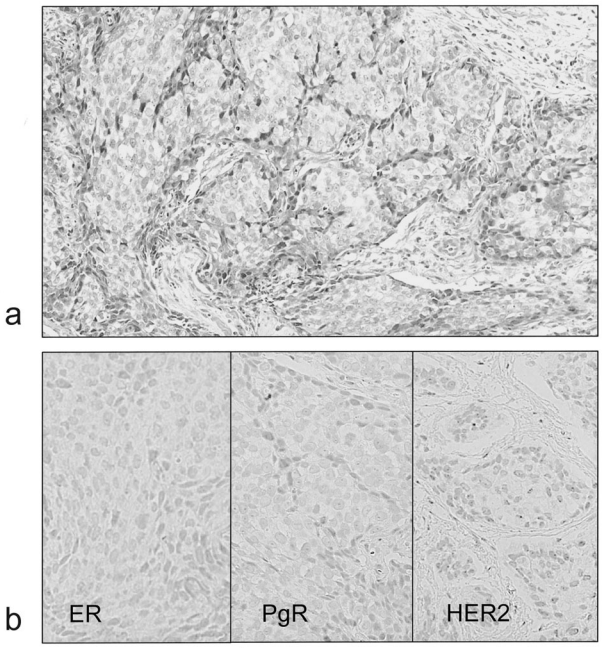

Figure 2. The histological findings of the chest wall tumor. (a) The section shows invasive ductal carcinoma with a solid-tubular growth pattern, indicated by hematoxylin and eosin staining. (b) Immunohistochemical staining showed that the tumor was ER negative, PgR negative and HER2 negative.

Discussion

The recurrence rates of breast cancer, according to the number of years since surgery, revealed a rate of 50% within the 2 years, and 83% within 5 years.[3] Although there have even been reports of recurrence in the chest wall in the vicinity of the surgical scar 40 years after mastectomy,[4]

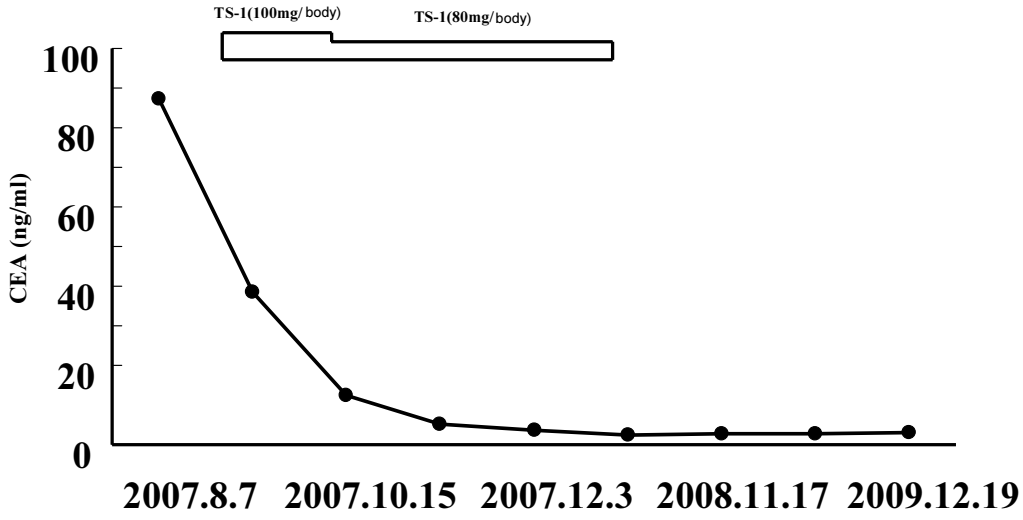

Figure 3. Changes in the serum CEA level with treatment.

approximately 80% of locoregional recurrence after mastectomy arises within the first 5 years.[5)]

The present patient was diagnosed with local recurrence in the chest wall 27 years after the surgery for breast cancer. Surgical resection is effective as a means of local control when there is isolated chest wall recurrence after mastectomy.[6)] Because the pectoral muscles of the present patient were removed previously, and because the tumor was large, a full thickness resection of the chest wall followed by reconstruction was thought to be necessary. That would have been an invasive procedure, especially for an elderly patient. The patient refused the surgery. Moreover, management of latent cancer cells that have yet to become prominent is always necessary with recurrent cancer. Approximately two-thirds of patients with local recurrence after mastectomy develop distant metastases.[6)] Since lymph node recurrence in the neck developed in our patient after the recurrence in the chest wall, a systemic therapy appeared to have been the right approach.

TS-1 is a novel oral anticancer drug that consists of a mixture of tegafur (FT), a prodrug of 5-fluorouracil (5-FU), and two biochemical modulators, 5-chloro2, 4-dihydroxypyridine (CDHP, gimeracil) and potassium oxonate (Oxo, oteracil).[7)] Gimeracil is a strong inhibitor of dihydropyrimidine dehydrogenase (DPD), and inhibits 5-FU degradation more effectively than uracil in vitro. Oteracil inhibits the phosphorylation of 5-FU. As oteracil is distributed in high concentrations in the gastrointestinal tract after oral administration, it decreases 5-FU-induced gastrointestinal tract toxicity. As a result, TS-1 is characterized by both augmented antitumor efficacy and reduced adverse effects. It was approved for manufacturing in January of 1999 in Japan, and indications were obtained for use against stomach cancer, head and neck cancer, colorectal cancer, and non-small cell lung cancer, but TS-1 is a relatively new drug to be used against breast cancer, with the indication having been expanded to include advanced or recurrent breast cancer in November 2005.

Anthracycline derivatives or taxane derivatives are currently key chemotherapeutic agents for breast cancer, but in addition to myelosuppression and alopecia, the anthracyclines often cause severe nausea and vomiting, and the taxanes are associated with allergic reactions, sensory disorders of the limbs, etc. These adverse effects make it difficult to continue treatment, and it is not uncommon for patients to experience a decline in their QOL. Our patient experienced general fatigue as an adverse effect of treatment with TS-1, but it was Grade 2, and the patient was able to continue with her daily life with only a minor decrease in QOL. Taira et al. have reported using TS-1 for 10 years in a single patient to treat recurrent breast cancer.[8)]

Triple negative-breast cancer is regarded as a highly malignant subtype of breast cancer, despite its increased sensitivity to standard chemotherapy regimens.[9)] In the present case, the reason for the excellent clinical efficacy exhibited by TS-1 may have been because the patient had no record of prior chemotherapy. Even after only 4 courses of TS-1, no re-enlargement has been observed as of the writing of this manuscript.

After our experience with this case, we believe that if no life-threatening metastases are present in patients with

recurrent breast cancer, treatment with TS-1 represents a feasible antitumor strategy with efficacy comparable to that of conventional chemotherapeutic agents that does not diminish a patient's QOL. TS-1 therapy appears to be an especially well suited for the treatment for elderly patients with metastatic or recurrent breast cancer. At present, a prospective trial (SELECT BC) that will compare TS-1 with taxanes in patients with metastatic or recurrent breast cancer is ongoing.[10] It is expected that the efficacy of TS-1 for metastatic or recurrent breast cancer will be equivalent to that of taxanes.

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