Positive Response to Oral Chemoendocrine Combination Therapy Using 5′-Deoxy-5-Fluorouridine for Locally Advanced Breast Cancer with Carcinomatous Pleurisy: Report of a Case

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Abstract
A 60-year-old postmenopausal woman presented with an ulcerating and bleeding tumor in her right breast. On physical examination, the tumor was found mainly in the D area of the right breast, and was associated with ulceration and thoracic rigidity. Chest X-ray showed a pleural effusion in her right chest and a computed tomography scan after thoracentesis showed multiple bilateral pleural nodules. Thus, a diagnosis of unresectable advanced breast cancer (T4cN2M1b, PLE) was made. She was given oral 5′-deoxy-5-fluorouridine (5′-DFUR) with medroxyprogesterone acetate (MPA) followed by tamoxifen, without any severe adverse reactions, and was subsequently followed up as an outpatient. Her tumor gradually decreased in size, the thoracic rigidity disappeared, and the pleural dissemination and effusion resolved. Thereafter, a radical mastectomy was performed and histologically, the tumor was Grade 1a. She had no signs of recurrence or metastasis 14 months postoperatively. Therefore, oral chemoendocrine combination therapy with 5′-DFUR resulted in a favorable quality of life, there were no severe adverse reactions, and the patient was able to be managed as an outpatient.

Key words 5′-Deoxy-5-fluorouridine · Locally advanced breast cancer · Oral chemoendocrine combination therapy

Introduction
The current drugs of choice for advanced or recurrent breast cancer include anthracycline and taxanes; however, these regimens sometimes show resistance and cause adverse reactions, such as cardiotoxicity, leukopenia, or alopecia, mainly due to doxorubicin. This obviously compromises the quality of life (QOL) of these patients.

Monotherapy with 5′-deoxy-5-fluorouridine (5′-DFUR) for breast cancer has been reported to result in a response rate of 35.9%; however, the concomitant administration of 5′-DFUR and medroxy progesterone acetate (MPA) increases the response rate to over 60%. This report describes the effectiveness of oral chemoendocrine combination therapy for treating and improving the QOL of a patient with locally advanced breast cancer associated with carcinomatous pleurisy.

Case Report
A 60-year-old postmenopausal woman first discovered a tumor in her right breast 4 years before seeking medical treatment. About 6 months before presenting, tumor ulceration developed, and intermittent bleeding started to occur about 4 weeks prior to admission, which she initially controlled with local pressure. At about the same time, she began to experience dyspnea on exertion and coughing. When she could not stop the bleeding, she visited our Department of Dermatology and was referred to us with suspected right breast cancer. Her past history was unremarkable. On physical examination we found a 60 × 50-mm ulceration in the DCEAB areas of the right breast (Fig. 1), a tumor associated with thoracic rigidity, oozing type bleeding from the ulcerative tumor, palpable rigid lymph nodes in the right axilla, and decreased right chest respirations. Her carbohydrate antigen (CA) 15–3 level was elevated to 113 U/ml and a massive right pleural effusion was found. She was admitted with a diagnosis of locally advanced breast cancer with bleeding. On admission, the bleeding site was compressed, intravenous anticoagulant therapy
was started, and right thoracentesis was done. A chest X-ray after the thoracentesis showed bilateral pleural hypertrophy and multiple nodules. The pleural fluid cytodiagnosis graded the cancer as class III. A computed tomography (CT) scan after the thoracentesis showed tumor invasion in the right thoracic wall (Fig. 2a) and multiple bilateral pleural nodules (Fig. 2b). These findings resulted in a diagnosis of locally advanced breast cancer associated with carcinomatous pleurisy (T4cN2M1b, PLE, Stage IV). Since the cancer was unresectable, we recommended intrathoracic injection of OK-432 and systemic chemotherapy. However, the patient did not consent to treatment and discharged herself about 3 weeks later. When we informed her about oral chemoendocrine combination therapy using 5'-DFUR, which is associated with less adverse drug reactions and is able to be given on an outpatient basis, we obtained her consent. She received oral 5'-DFUR, 800mg/day, and MPA, 800mg/day. About 6 weeks after starting the treatment, the tumor ulceration gradually decreased to 30 × 20 mm in size and her CA15-3 level dropped to 27 U/ml. However, blood coagulation system abnormalities were evident by increases in α2-PIPM and fibrin degradation products. To avoid the risk of thrombosis, MPA was replaced by tamoxifen (TAM), 20mg/day. By 6 months after starting the oral treatment, both the ulceration and the thoracic rigidity had disappeared, although the pectoral muscle rigidity remained (Fig. 3). Her tumor markers became normal, and no nodules or pleural fluid effusions were found on chest X-ray or CT Examination (Fig. 4a,b). She

Fig. 1. The advanced right breast tumor with a 60 × 50-mm ulceration associated with thoracic rigidity

Fig. 2. Computed tomography after right thoracentesis showed tumor invasion in the right thoracic wall (a) and multiple bilateral pleural nodules (b)

Fig. 3. The breast tumor 6 months after starting treatment. The ulceration and thoracic rigidity had disappeared, but the pectoral muscle rigidity remained