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A Case of Inflammatory-Edematous Breast Cancer Treated with Combination Therapy

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Abstract

Objectives: Current breast cancer treatment involves both standard (e.g., surgery, chemotherapy radiation therapy, and hormone therapy) and new immune therapy methods. Standard treatments are effective at early stages but their effectiveness drops with advanced stages. Recent studies suggest that bacterial and viral infection could be implicated in breast cancer pathogenesis. Therefore, pathogenic inhibition could be a feasible treatment approach.

A 54-year-old woman presented with an inflammatory-edematous form of breast cancer (T4N1M1 stage). Due to the inflammatory edematous form tumor was fully metastasized and inoperable. Patients with similar condition usually have a very short life span.

Methods: This patient underwent a combinatorial therapy consisting of immunocorrective and metabolism regulating therapy, as well as antimicrobial and standard chemotherapy.

Results: This treatment was shown to extend patient's life for almost two additional years. This case report demonstrates extent and possibility of using a systemic approach to treat inoperable breast cancer.

Keywords: Breast cancer; Combinatorial therapy; Immunocorrective therapy; Antimicrobial therapy; Antiviral therapy

Introduction

Breast cancer is now the most common cancer type in both developed and developing countries, accounting for a quarter of all cancers in women [1]. The development of breast cancer is associated with numerous internal and external factors that play a major role during initiation, development, and progression of this disorder.

The International Agency for Research on Cancer stated that 18-20% of cancers are linked to infection, and the list of definite, probable, and possible carcinogenic agents is growing each year [2]. Several reviews have comprehensively summarized the role of infections during carcinogenesis in several types of cancers [3-5] with many studies associating breast cancer with human cytomegalovirus (HCMV) [6,7] and Epstein Barr virus (EBV) [8-10] of the Hepesviridae family.

Current results show that anticancer cytotoxic agents used in chemotherapy cause a decrease in the number of functional white blood cells, red blood cells, and platelets. Clinical manifestations of immunosuppression are caused by the activation of latent infections. The presence of such infections following chemotherapy frequently promotes tumor re-growth and the development of secondary neoplasms [11]. It is becoming obvious that well known cancer treatments for metastasized breast cancer have a strong limiting factor and that this treatment modality at the present time needs further improvement. A combination of systemic immune therapies with well-studied and commonly used cancer therapeutic agents together with antinfectious agents should therefore be considered for possible treatment of cancer.

The present report presents a treatment strategy for cases of inoperable and aggressive forms of breast cancer with a background of various infections, as well as severe immunosuppression. Usually a patient presenting with a severe inflammatory-edematous form of breast cancer would not be expected to survive surgical intervention. Hence, our treatment strategy used a different approach based on pathogenic inhibition and systemic correction of the biological, immunological, and metabolic effects of carcinogenesis.

Case Presentation

A 54-year-old woman was admitted to our hospital (Republican scientific center for emergency care) in June 2011 with lower back pain and general fatigue. Her skin and visible mucous membranes were pale with a gray shade.

Prior admission to our hospital, in January, 2011, she felt intense pain in her lower back and noticed palpable node formation in her left breast a few months later. She was diagnosed with inflammatory-edematous breast cancer at T4N1M1 stage in Oncology hospital of Astana. Computer tomography and cytological analyses revealed adenocarcinoma and several metastases. The patient was treated with beam-therapy, chemotherapy (chemotherapy regimen included paclitaxel 300 mg + Adrim), and palliative analgesic gamma teletherapy on compressed vertebrae L II. Chemotherapy showed high toxicity and led to further deterioration of the patient, accompanied by fast spreading metastases. She received the score of 20 according to Karnofsky Performance Status Scale which is close to preterminal condition. Since neither chemotherapy nor beam-therapy was found effective and the patient was diagnosed to be incurable, an alternative

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treatment strategy that includes combination of adjuvant and standard chemotherapy was proposed after being admitted to our hospital.

Methods

Diagnosis methods

Before starting treatment, overall medical condition of the patient was observed, computer tomography, magnetic resonance imaging, immunogram, serological analysis were performed.

Therapy methods

Due to the above mentioned complications at admission, this patient underwent a personalized systemic treatment rather than the targeting of localized tumors. Limitations of standard breast cancer treatment methods in this case indicated that treatment should focus more on restoring the patient's immune system at the very first stages of treatment instead of downregulating it via chemo- and/or radiotherapy.

We first performed adjuvant therapy in order to restore normal functions of the immune system, then we used chemotherapeutic drugs. Details of treatment are shown in Tables 1 and 2. The patient had elevated titers for infections, therefore the treatment strategy included antiviral, antibacterial, and antifungal drugs. Considering impaired levels of immune components of the blood, the patient was also given immunomodulating therapy, which included interferons and interleukins, which improved blood test results significantly during the treatment. She was also given metabolic syndrome restoration therapy (hypoglycemic and lipid metabolism-regulating drugs). After complex restoration therapy the patient underwent low dose chemotherapy with Xeloda and Doxorubicin, which did not show any toxic effects.

08.06.2011-15.03.2012
Lipanthyl 0.2 gr during lunch
Liprimar 20 mg during dinner
Viferon 3 mln, rectally, morning/evening
Bifidumbacterin 3×day
Valtrex 0.5 gr 2×day
Adapton 1 tablet before sleep
Calcium-D3 Nycomed 2×day
Tamoxifen 40 mg 1×day
Glutargin
Polyvitamin complex

Table 1: Anti-cancer immune therapy, antiviral therapy, metabolic syndrome restoration, antibacterial therapy.

25.04.2012-05.06.2012
Roncoleukin (recombinant human IL2)
Alfa-Feron 3 mln (Interferon alfa)
Tamoxifen 20 mg 1×day
Adapton 1 tablet before sleep
Famvir 0.5 1 tablet, 2×day
Pylobact Neo 3 tablets 2×day
Bifidumbacterin 3×day
Liprimar 20 mg during dinner
Glucophage 0.5 1 tablet before sleep
Zometa (zoledronic acid) 4 mg
Calcium-D3 Nycomed 2×day

Table 2: Treatment with chemotherapeutic drugs.

Test	Cut-off value (OD)	Result (OD)
Rubella virus IgG	0.254	0.796
EBV type I (VCAIgG)	0.157	3.000
CMV type I IgG	0.121	2.000
HHV I and HHV 2 IgG	0.120	3.000

Table 3: Serological analyses showed elevated titers of antibodies for several viruses.

Cellular immunity parameters, absolute (10^9/liter)	Reference	June, 2011	July, 2011	March, 2012
T-lymphocytes (CD3+CD19-)	0.8-2.2	0.154	0.171	0.308
B-lymphocytes (CD3-CD19+)	0.1-0.6	0.04	0.046	0.264
T helper (CD4+CD8-)	0.4-1.1	0.099	0.079	0.202
T cytotoxic (CD4-CD8+)	0.3-0.7	0.063	0.079	0.246
Immuno-regulatory index (IRI)	1.2-2.0	1.5	1.0	0.8

Table 4: Analyses of the patient's blood revealed decreased levels of immune cells.

Results

Diagnosis results

Breast examination revealed a round-shaped formation 9 cm in diameter in the center of her left breast. The breast was edematous. The formation was rigid and painless, with skin around it diffusely thickened. Computer tomography showed multicentric growth of an adenocarcinoma. The nipple was inverted. Movable conglomerate of lymph nodes with tight elastic consistency 2 cm in diameter was in the left axillary area. Cytological analysis revealed adenocarcinoma in the left breast, and metastasis in the left axillary area.

Computer tomography and MRI were performed in order to evaluate spread of metastasis. Computer tomography showed extensive multiple metastases in the form of osteolytic destructions in the body of thoracic vertebrae; in the body and lamina of lumbar vertebrae LI, II, III, IV, V (body of LII vertebra was compressed) and sacral vertebra SI; in the handle and body of sternum; in pelvic bones; in the right scapula; in ribs 4, 5, 6 on the right side and 7 on the left. Metastases occurred in lymphatic nodes of mediastinum and in both lungs (miliary carcinomatosis). Computer tomography of the abdomen showed metastatic lesions of body and the right arch of vertebrae L1, body of L2 vertebrae, right posterior vertebral arch, L3 vertebrae, arch, spinous process, bodies of L4, and L5 vertebrae. There were signs of pathological compression fracture of the body of L2, and Phase 1 of the right-sided scoliosis of the lower thoracic and lumbar vertebrae. Magnetic resonance imaging of the pelvis showed adenomyosis of the uterus, and multiple metastatic lesions of the bodies of vertebrae L3, L4, L5, S1, and pelvis bones.

Serological analyses showed elevated titers of antibodies for several viruses (Table 3) and highly elevated levels of total antibodies for Helicobacter pylori (1:20), *Mycoplasma hominis* IgG (1:10), and *Chlamydia trachomatis* IgG (1:5). Immunochemiluminescent assay of blood serum was positive for *Toxoplasma gondii* IgG. Analyses of the patient's blood revealed decreased levels of immune cells (Table 4).

Patient was tested HIV-negative and did not have connective tissue disorder or lupus like disease.

The immuno-regulatory index was within the normal range, however the overall level of immune cells was lower than normal ranges. In addition, the patient had concomitant diseases such as metabolic syndrome, hepatosis, chronic pancreatitis, and gastritis. Magnetic resonance tomography of pelvic organs suggested the existence of endometrial cysts in the uterus.

Treatment results

Within two months after starting treatment, computed tomography of thorax and abdomen showed no additional destruction sites and no further spreading of overall metastasis. After about six months of treatment, mammography results showed positive dynamics compared to what was obtained initially, and there was decreased infiltration of the left mammary gland. Cytological analysis showed the absence of malignant cells at the primary tumor site. Moreover, no new sites of metastasis were observed. According to Karnofsky Performance Status Scale, the patient scored 80-90.

On 07/12/2012, the patient discontinued treatment and returned to work. The patient declined assignment to a disability group. She returned in February 2013 with new metastases in both lungs, and she died in March 2013.

Discussion

When admitted to our hospital, the patient had terminal stages of inflammatory breast cancer with edematous swelling and multiple metastases in bones, lungs, and lymph nodes, which continued to spread throughout the body. In addition, the patient's immune system was impaired, with the presence of multiple infections, chronic gastritis, and pancreatitis, and the patient was expected to live 2-3 months at most. However, it was possible to stop further spreading and development of metastases with combinatory treatment, which included immune supportive, antiviral, and antibacterial therapies, as well as correction of metabolic syndrome, followed by chemotherapy. Toxic effects of chemotherapy were not observed due to combination treatment. Relief from pain syndrome, improvement of overall condition and well-being were noted (up to 80-90% using the Karnofsky Performance Status Scale), as the patient was able to take care of herself and returned to work.

However due to discontinuation of the treatment, the patient's condition worsened and multiple new metastases spread throughout the upper body and lymph nodes, concentrating in the lungs. Our treatment extended her life for almost two years when she was expected to live for three months at most. We believe there would have been a better outcome if the patient was admitted earlier, before development of systemic metastases, and if the treatment was not discontinued.

Conclusion

Treatment of patient with inflammatory-edematous breast cancer at T4N1M1 stage with standard chemotherapy was not effective and she was classified as incurable. Since we believe that it is very difficult to treat cancer without treating the underlying diseases, the scheme of treatment was changed to include both ethiotropic and adjuvant therapies. As a result of this treatment strategy, it was possible to stop further spreading and development of metastases. The overall condition of the patient was improved as shown by increase of the Karnofsky Performance Status Score from 20 to 80-90. Unfortunately, discontinuation of treatment lead to further spread of metastasis and patient died. Our treatment had no fixed program, but was flexible depending on the patient's immune profile, chronic and acute infections, and any concomitant diseases such as metabolic disorders. Nevertheless it requires further optimization and studying. We therefore suggest that personalized treatment should become a main approach to treat cancer patients.

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