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Relapses following adjuvant anthracycline containing regimens in high-risk operable breast cancer

KEYWORDS: Breast cancer; Anthracyclines; Recurrence

The primary resistance to anthracycline seemed to be the predictor of subsequent treatment failure and shorter overall survival in metastatic breast cancer. However, the primary resistance to anthracyclines, used in adjuvant settings, could not be easily recognized, except in the case when the recurrent disease occurred while on the adjuvant treatment, or immediately after its completion. To estimate the relation of DFI with the subsequent treatment response and the overall survival in BC patients who were treated with adjuvant anthracycline (A) chemotherapy in Clinic of Oncology, Podgorica, during the period 1995-2000. Hospital files of 20 operable BC patients treated with adjuvant anthracycline-containing regimens, were reviewed (pre- and postmenopausal;median age 43, range 30-65). Related to patients' age, tumor size or grade, and nodal status, all patients belonged to the high-risk group. Steroid receptors were not routinely determined. The used adjuvant A regimens were AC, FAC or "sequential", with or without subsequent endocrine therapy. All patients relapsed, having been treated afterwards with various chemotherapy regimens, including paclitaxel, gemcitabine, Xeloda and CDDP. The most frequent first relapse sites were viscera and soft tissue (10 and 6 patiens, respectively), multiple in 2 patients, while bone metastatic involvement was infrequent. Related to disease free interval (DFI), patients were subgrouped in 2 subsets: DFI≤6 months (5 patients), and DFI>6 months (15 patients). Thus, 5/20 patients (25%) could be considered as primary anthracycline-resistant BC, since they relapsed either while on chemotherapy, or immediately after its completion. 1/5 patient responded to subsequent treatment of metastatic disease, and their overall survival ranged from 7-22 months. On the contrary, some of the patients with the DFI>6 months responded to either subsequent endocrine or chemotherapy, 4/20 having been still alive. These results confirmed the relation between the early failure to adjuvant anthracycline chemotherapy and subsequent treatment failure, in unfavorable group of early BC patients.

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Postanthracycline therapy with the combination of Herceptin/Taxol (H/T) treatment of metastatic breast cancer (case report)

KEYWORDS: Breast cancer; Neoplasm, metastases; Trastuzumab; Paclitaxel

The aim of the work was to present the role of "salvage" therapy H/T in postanthracycline treatment of metastatic breast cancer. In this work a case of female patient V. R. aged 63, treated for disseminated breast disease at the Institute of Oncology was reported. The patient underwent left side mastectomy in1998 due to tumor classified as T2, N0, M0, after which she was treated with adjuvant chemo-radiotherapy. During 2000, due to metastatic skeletal lesions, she received series of FAC protocol, after which endoprosthesis was implanted due to pathologic fracture of acetabulum. In March 2001, the MRI examination revealed dissemination of the disease in the endocranium and ultrasound examination revealed multiple liver lesions. Accordingly, a palliative irradiation of the brain was performed, and a therapy according to protocol H/T, with addition of Lomustin was introduced. After the VII applied series of Taxol with weekly administration of Herceptin, the MRI of endocranium did not indicate the presence of secondary deposits and liver MRI was in normal ranges. This effect was followed by the general improvement of patient's condition with mild toxic side effects. The results of this work are indicative and indicate the need for earlier diagnostics of disease dissemination for more efficient therapeutical approach. Beneficial effect of H/T therapy in patients previously treated with anthracycline therapy proves, that despite dissemination of the underlying disease, such approach in the treatment may result in remission of the disease.

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Toxicity profile of Xeloda in pretreated patients with breast cancer

KEYWORDS: Breast cancer; Chemotherapy; Toxicity; Capecitabine

The new tumor selective fluoropyrimidine - Xeloda (capecitabine) demonstrated activity especially in breast cancer. The purpose of study was to determinate toxicity profile in heavily pretreated patients with breast cancer. Patients and method: Xeloda was administrated in the outpatient setting and given orally at a dose of 2500 mg/m^2 per day, divide in two doses for 4 days, followed by seven days rest. This schedule was repeated in three-week cycles. We evaluated 18 patients with locally advanced or metastatic breast cancer. The median age was 58.3 (range 40-69). The patients received 4 to 8 cycles of Xeloda with only mild to moderate adverse events. The most common treatment related NCI CTC toxicities were hand and foot syndrome in 3 patients (16 %), stomatitis in 3 patients (16 %), nausea and vomiting in 4 patients (22 %) and diarrhea (24% grade 2=12%, grade 3=12%). Grade 3/4 toxicities occurred in less than 7 % of patients. Leukopenia was noted in 5 patients (27%) and thrombocytopenia in 1 patient (5.5%). No grade 3/4 myelosuppression was reported. All these events were manageable by dose reduction or therapy interruption. The mean number of prior therapies in our group was: chemotherapy regiments 2(CMF and CAF) and chemotherapy agents 4.3 (anthracyclines included). In the whole number of patients treated with Xeloda 80 % was heavily pretreated. Visceral metastases were predominant (liver 93%, two metastatic localizations 26,6%). Neither alopecia nor death related to Xeloda was noted. Despite that almost whole group was heavily pretreated the toxicity profile is acceptable and easy manageable.

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Mitomycin C in the treatment of advanced breast cancer patients, previously exposed to antracyclines

KEYWORDS: Breast cancer; Cytotoxic drug therapy; Anthracyclines; Mitomycin; Drug resistance

Doxorubicin is included in standard chemotherapy regimens of advanced breast cancer, either as a first- or second-line treatment. Due to its efficacy in metastatic disease, it is also frequently used in adjuvant treatment, at least in high-risk early breast cancer patients. It is generally believed that patients relapsing after doxorubicin treatment have a poor prognosis, due to the multidrug resistance. Many innovative drugs are in the development or in clinical research, with the aim to find out the best post-anthracycline regimen. However, the role of well-known drugs and regimens could also be of interest in post-anthracycline treatment of metastatic breast cancer. Mitomycin C is one of such drugs. During the period from 1997 to 2000, 25 advanced breast cancer patients were treated with Mitomycin C, either alone (12/25) or in combination with vinblastine, methotrexate and/or Mitoxantrone. All patients had been previously treated with doxorubicin, mostly with FAC regimen, either as adjuvant treatment, or systemic therapy for metastatic disease (12 and 13 patients, respectively). Obtained response rate to Mitomycin C-containing chemotherapy was: 6/24 (24%) partial remissions, with additional 28% disease stabilizations. Objective response was related to the overall patients' condition. Additionally, when the time period between the termination of doxorubicin treatment and introduction of Mitomycin C regimen was longer than 24 months, the response was somewhat more frequently obtained. Mean survival from the introduction of Mitomycin C-containing chemotherapy was longer when the period between anthracycline and Mitomycin C treatment was longer than 24 months, and, in addition, it was influenced by the response to Mitomycin C regimens. In conclusion, it seems that there exists a subpopulation of patients pre-treated with doxorubicin-containing chemotherapy, which does not express the multidrug cross-resistance. It could be useful to concern Mitomycin C-containing regimens for those patients. Our results suggest that the time interval between doxorubicin and Mitomycin C chemotherapy could be the selection criterion.

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Postanthracycline therapy in metastatic breast cancer patients - a single center experience

KEYWORDS: Breast cancer; Neoplasm, metastases; Anthracyclines; Salvage therapy; Antineoplastic agents, combined

This paper deals with the analysis of the efficacy of postanthracycline therapy in 22 advanced breast cancer patients who had been treated during the period from 1992 to 2001. The average age was 44 years (range 31-61 years), 12 out of 22 patients were premenopausal, 10/22 women were postmenopausal, and steroid receptor content of primary tumors was unknown for the majority of them (3/22 had SR negative, while 4/22 women had SR positive tumors). Fifteen out of twenty patients who had been operated on for early breast cancer received adjuvant chemotherapy that contained cyclophosphamide, methotrexat and 5-fluorouracil. Median disease free period for all twenty patients was 26 months (range 14-89 months). All 22 women received anthracycline-containing chemotherapy as first-line therapy for metastatic disease, and the median response duration was 9 months. After disease progression 6 out of 22 patients received second-line chemotherapy that contained cisplatin, cyclophosphamide, methotrexat and fluorouracil (PCMF), while the remaining women were treated with endocrine therapy. The median response duration to second-line therapy was 8 months including all patients. Second-line therapy showed greater activity in patients with lung and soft tissue lesions than in women with liver metastases. Median survival for the whole group was 60 months (range 20 - 125 months).

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Endocrine responsiveness in an advanced breast cancer patient, pre-treated with doxorubicin: A case report

KEYWORDS: Breast cancer; Liver; Neoplasm, metastases; Antineoplastic agents, hormonal

The female patient B. M., aged 36, was mastectomized in Medical Center Užice, in January 1994 for stage IIa invasive ductal breast cancer, histology grade 2, with involved 7/14 left axillary lymph nodes. Steroid receptors were not determined. The adjuvant CMF x6 chemotherapy was applied followed by castration by irradiation. After a DFI, lasting 24 months, echotomography and CT scan showed multiple liver metastases. A low dose FAC chemotherapy regimen was introduced (50 mg Adriamycin/ per cycle). Only a minor decrease in focal liver lesions diameter was noted, the response was classified as SD. Chemotherapy was terminated after 12 cycles. Since there was no signs of further dissemination, and the patient's preference was to discontinue the chemotherapy, a maintaining endocrine therapy with tamoxifen was prescribed. Six months later, Echo and CT scans confirmed the complete regression of liver lesions, which lasted till January 2001 (39 months), while the patient continuously have been under tamoxifen treatment. Then, the new relapse occurred, with recurrent hepatic and bone involvement. The case of this young woman is rather unusual, due to several points. First, this was obviously an endocrine dependent disease, according to the unexpected response to tamoxifen. In the same time, the aggressive tumor growth can be supposed, based on the patient's age, initial histology and later first relapse presentation. The minor response to FAC chemotherapy probably could be ascribed to the low-dose doxorubicin regimen. However, the anthracycline resistance could not be excluded, depending on the definition. Although the endocrine responsiveness could be compromised by the previous use of chemotherapy, probably due to the loss of steroid receptors, obviously this was not the case. In addition, it was suggested that receptor-negative tumor cell clones tended to metastasize into the viscera, decreasing the probability of responsiveness to endocrine manipulations. Thus, the quality of the obtained response to tamoxifen was unusual per se. The presented case confirms that endocrine therapy should be carefully considered for individual patients, even for younger ones, those supposed to have the aggressive tumors and/or the unfavorable clinical presentation.

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Chemotherapy of breast cancer in relapse following anthracycline-containing adjuvant treatment

KEYWORDS: Breast cancer; Anthracyclines; Recurrence; Salvage therapy; Survival

From 1989 to1999 the Oncology Outpatient Center Leskovac registered 193 patients with breast cancer who died of their disease. Sixty-six (34.5%) of them were treated with the CAF regimen. Twenty-five (37.8%) developed metastatic disease: 7 patients (28%) in the liver, 5 patients (20%) in bones, 8 patients (32%) in lungs and 5 patients (20%) had a local relapse. For that reason 5 (20%) patients were treated with the CMF regimen, 17 (68%) with MITC and 3 (12%) with the AP regimen. In patients treated with CMF regimen, 6-month survival period was 60%; 12-month survival period was 40%. In patients treated with MITC regimen, 6-month survival period was 82%, 12-month survival period was17.7%. In patients treated with AP regimen, 6-month survival was 100%. Total survival period of patients treated with postanthracycline chemotherapy for 2-year period was 88.8%, for 3 years 40%, for 4 years 16% and for 5 years 4%. If the disease free period is short, then therapeutic response is dissatisfactory. In our case 62.2% of patients treated with anthracyclines didn't have any progression, which made very good therapeutic response. The longest survival in relapsed patients was achieved with CMF but the results are far from satisfactory.

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Docetaxel in anthracycline-and Paclitaxel pretreated metastatic breast cancer (MBC) patients-is it active?

KEYWORDS: Breast cancer; Neoplasm, metastases; Paclitaxel; Salvage therapy; Docetaxel

Our first encouraging results using docetaxel in paclitaxel pretreated MBC patients (Abstract book 25th ESMO Congress, Hamburg 2000) have had induced us to establish this as a standard "next step" chemotherapy in treatments of our MBC patients. Up to August 2001, 27 patients were treated in this way. Pretreatment included adjuvant CMF therapy and anthracycline as the first-line treatment for metastatic disease. Four patients received PCMF as the second-line and three patients received MV protocol as the third-line chemotherapy. All patients were treated with paclitaxel (as monotherapy or in combination with cisplatinum) as well. After the treatment failed, all patients received docetaxel (Taxotere®) as monotherapy (100 mg/m^2 1h IV day 1, q 3 weeks). Adequate premedication was applied. Six patients were treated on outpatient's basis. Median age was 51 (38-62) years. Thirteen (48.1%) patients were premenopausal and fourteen (51.9%) postmenopausal. Twenty-three (85.2%) patients had two or more metastatic lesions. With eleven (40.7%) patients liver was dominant metastatic site. All patients were evaluable for response and toxicity. A total of 131 chemotherapy courses were administered, with a median of 4 cycles per patient (range 3-6). Response so far included two (7.4%) CR and fourteen (51.9%) PR for ORR of 59.3% (95%CI 56.6-85.4). SD occurred in another four (14.8%) patients accounting for a tumor control rate of 74.1%. In seven (25.9 %) patients PD was observed. Best response was seen in patients with liver metastases (54 %). Neutropenia grade 3 was observed in five (18.5 %) and grade 4 in two (7.4 %) patients. None of patients had a febrile neutropenia. Grade 3 thrombocytopenia developed in four (14.8 %) patients. Grade 4 was not observed. Non-hematological toxicity was mild. Docetaxel is active in anthracycline- and paclitaxel pretreated MBC, resulting in an ORR of 59.3% and tumor control rate of 74.1%. This treatment was generally well tolerated and can be safely used on outpatient basis. Our data confirm an incomplete cross-resistance between docetaxel and paclitaxel.