

BREAST CANCER AS A SECOND TUMOR AFTER RADIOTHERAPY IN PATIENT WITH HODGKIN'S LYMPHOMA-CASE REPORT AND LITERATURE REVIEW

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Cancer induction after radiation therapy is known as a serious side effect.

We present a female patient with breast cancer as a second malignancy after Hodgkin disease treatment, twelve years after the disease was detected. A Core Needle Biopsy was performed and a breast cancer was confirmed. The patient underwent neoadjuvant chemotherapy and preoperative radiotherapy to the right breast. After that, a radical right mastectomy was done, with a right axillary dissection. Subsequent histopathological examination revealed an invasive intraductal breast carcinoma.

It is important to point out that there are potential risks and long-term complications of anticancer therapy among cancer survivors. *Acta Medica Medianae* 2017;56(1):71-74.

Key words: *Hodgkin's lymphoma, breast cancer, second malignancy*

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Second malignancy after Hodgkin disease was first recognized as a problem in the early 1970s (4, 5). Breast cancer is the most common solid tumor that develops in women following combined curative treatment with chemo- and radiotherapy for HD (6).

Aim

In this paper we present a female patient with breast cancer as a second malignancy after Hodgkin disease treatment, twelve years after the disease was detected.

Case report

In May 2002, a 14-year-old, previously healthy female was admitted to the General Hospital "Studenica" in Kraljevo because of a two-week history of a painless enlargement of the left supraclavicular lymph nodes. The enlarged, hard lymph node, the size of a walnut, painful on palpation, was revealed in the left supraclavicular area during the physical examination. Computed tomography (CT) of the chest showed a para-aortic, 5x3 cm soft tissue mass in the anterior mediastinum. An excisional biopsy of the enlarged lymph node and the histopathological (HP) examination of the tissue were performed. Based on the examinations that included biochemical analysis, chest X-ray and CT scan, abdominal ultrasound, an excisional biopsy of the enlarged lymph node and HP verification, the diagnosis of IIA Hodgkin's lymphoma was made. The patient

Introduction

Hodgkin's lymphoma (HL) has been increasingly common among children and young adults both in Europe and the U.S. (1), with a slightly higher incidence in men than in women. Young adults aged 20–40 years are the ones most commonly affected, and a second incidence peak is seen in individuals aged 55 years and older (2).

Radiation therapy (RT) is most useful when Hodgkin disease is affecting only one part of the body. For this disease, radiation is often given after chemotherapy, especially when there is a large tumor mass (usually in the chest). This combined modality treatment was shown to result in superior tumor control compared with RT alone (2). Cancer induction after radiation therapy is known as a severe side effect (3).

was treated with 6 cycles of chemotherapy according to ABVD protocol and with radiotherapy after the completion of chemotherapy, after which the patient achieved complete remission.

In 2011, she had a delivery by Caesarean section. The pregnancy was normal.

In June 2014, the patient was admitted to the General Hospital Novi Pazar because of a swelling in her right armpit and a palpable breast mass in the right upper outer quadrant, both discovered during a medical checkup. A Core Needle Biopsy was performed and a breast cancer was confirmed (i.e., cancer cells were detected). The patient underwent neo-adjuvant chemotherapy with Taxolom, after which preoperative radiotherapy was applied on the right breast. After that a radical right mastectomy was done, according to Madden, with the dissection of the right axilla. Subsequent histopathological examination established an invasive intraductal breast carcinoma, histological gradus III and nuclear gradus III; Estrogen score: 4 (less than 1%); Progesteron score: 0; HER2: 1+; Ki67: high (75%) and metastasis to one of the axillary lymph nodes. Consequently, the patient received adjuvant treatment with Goserelin acetat (Zoladex) and Tamoxifen (Nolvadex).

During the follow-up period there was not any recorded recurrence or metastasis.

Discussion

The overall survival for Hodgkin's lymphoma (HL) has improved significantly in the last 25 years, and the treatment of this curable malignancy has continued to evolve due to improvements in the treatment techniques (7). Radiotherapy is important in the treatment of Hodgkin lymphoma. Although the risk of recurrent Hodgkin lymphoma decreases in long-term survivors, the incidence of radiation-induced cancers in children treated for Hodgkin lymphoma increases with time. Many long-term studies have demonstrated that girls and young women treated with chest radiotherapy for Hodgkin lymphoma have a significantly greater risk of developing breast cancer, compared with the general population (8).

Swerdlow et al. have found that the cumulative risks for these patients is up to 48% to develop a breast cancer up to 40 years after treatment and the age of treated patients, field of RT, and treatment with chemotherapy (CT) have been identified as factors that affect this risk (9).

According to Walner-Roedler DL et al., the risk of developing breast cancer is limited to women treated before 30 years of age with the median time of 15 years to breast cancer after radiotherapy. Higher radiation doses are associated with higher risks (10).

Elkin EB et al. found that in women treated for HL before 30 years of age, the risk of developing breast cancer is six times greater than in the general population (11). In this study they found

that the median age at HL diagnosis was 23 years, and the median interval from HL to first breast cancer diagnosis was 18 years (11).

The study of Veit-Rubin N et al. (1) also confirmed these findings. It is a well known fact that breast tissue sensitivity to ionizing radiation is higher in younger patients (12). In their study, 32% of patients with BC following HL were below 40 years of age, compared with 7% of BC patients without a history of HL (1, 12). Women with HL after the age of 50 did not have a higher risk for a second BC (1). Veit-Rubin N et al. reported that BC after HL occurred more frequently in external breast quadrants. Some older studies reported a highed incidence of tumors in the inner quadrants (1, 13).

Horst KC et al. suggested that radiation-associated BCs may have a more aggressive biologic profile than those arising in nonirradiated breast tissue (8).

A breast cancer in young patients is likely to display a more aggressive phenotype, to be hormone receptor negative, and to exhibit more vascular and lymphatic invasion and pathologic grade 3 features (8, 14).

Castiglioni et al. reported that BCs arising after irradiation were less likely to be ER and PR positive compared with a control group of sporadic BCs. This study suggested that radiation administered during breast maturation can be a risk factor for the development of HER2-overexpressing breast carcinomas presenting amplification of the HER2 oncogene (15).

The study of Horst et al. suggested that in patients previously irradiated for HL, invasive cancers were more likely to be hormone receptor (HR)-/HER2- and less likely to be HR+/HER2-, compared with invasive cancers that developed in the sporadic cohort (8). They found that invasive BCs arising in previously irradiated breast tissue were more likely to be triple-negative compared with age matched sporadic invasive BCs (8).

Similar results were obtained by Dores et al. in a population-based study which suggested that long-term survivors of HL treated with RT before 35 years of age have a significantly higher risk of developing ER-negative/PR-negative than ER-positive/PR-positive BC (particularly those surviving 15 years). Fifteen-year HL survivors also had a significantly higher risk of developing high-grade than low-grade tumours (16). Moreover, there was a high incidence of both synchronous and metachronous bilateral breast cancer in patients who received radiotherapy for HL (11, 17).

Lifelong specialist follow-up of women irradiated for Hodgkin's disease should be considered; monthly self-examination of the breasts should be advised and mammography should be carried out annually 10 years and more after thoracic or axillary irradiation. It is especially the women treated before their 20th year of life who run a relatively high risk (18, 19). These women did not have better breast cancer outcomes than their peers with sporadic breast cancer (11).

Comparing the women with breast cancer after either HL or non-Hodgkin's lymphoma with those with sporadic breast cancers matched for age, stage, and year of diagnosis, 5-year disease-free survival was only 54% in lymphoma survivors compared with 91% in the comparison group (20).

Based on their concerns about possible severe consequences arising after a high total cumulative dose of radiation to the breast, several authors have suggested mastectomy as the treatment of choice for BC after HL (21-23). The decision whether to administer RT following mastectomy should be individualized, with a careful consideration of the benefits and potential toxicity for each individual patient (22).

Conclusion

In conclusion, the fact has to be emphasized that there are potential risks and long-term complications of anticancer therapy among cancer survivors. Therefore, we should continue to develop screening strategies for individuals who have survived cancer, to educate our patients and promote preventive strategies among cancer survivors.

Conflict of interest disclosures

The authors confirm that no conflict of interest exists in relation to this article

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**UDC: 618.19-006:[616.42-006.44:615.849
doi:10.5633/amm.2017.0111**

KARCINOM DOJKE KAO SEKUNDARNI TUMOR NAKON RADIOTERAPIJE KOD BOLESNICE SA HOČKINOVIM LIMFOMOM: PRIKAZ SLUČAJA I PREGLED LITERATURE

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Karcinom indukovan prethodnom zračnom terapijom predstavlja tešku komplikaciju ovakvog lečenja.

Predstavljamo bolesnicu s karcinomom dojke, koji se razvio nakon lečenja Hočkinove bolesti, dvanaest godina nakon sto je bolest detektovana. Karcinom dojke je otkriven nakon Core biopsije dojke. Bolesnica je lečena neo-adjuvantnom hemoterapijom i preoperativnom radio terapijom desne dojke. Nakon toga je učinjena radikalna mastektomija desne dojke uz disekciju desne aksile. Nakon histopatološke obrade tkiva, potvrđen je invazivni duktalni karcinom dojke. Važno je istaknuti da postoje potencijalni rizici i dugoročne komplikacije antitumorske terapije kod preživelih bolesnika lečenih od karcinoma. *Acta Medica Medianae* 2017;56(1):71-74.

Ključne reči: *Hočkinov limfom, karcinom dojke, sekundarni malignitet*

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