THE INSTITUTE OF ONCOLOGY, LJUBLJANA

TRIPLE CARCINOMA IN A PATIENT WITH PRIMARY BREAST CANCER

Čufer T, Cerar O

Abstract – The case of a patient with triple malignoma is reported. On surgery for primary breast carcinoma the pathohistologic examination of the removed axillary lymph nodes revealed the presence of non-Hodgkin lymphoma of low-grade malignancy. Further clinical, laboratory and diagnostic investigations confirmed that, apart from breast cancer, the patient also had a non-Hodgkin lymphoma of KLL type, stage IV A. Two years later, an invasive transitional cell carcinoma of the pyelon of the right kidney was diagnosed as well. The incidence of multiple primary neoplasms in patients with primary breast cancer is discussed.

UDC: 618.19-006.6-06

Key words: breast neoplasms, neoplasms multiple primary, lymphoma non-Hodgkin's, kidney neoplasms

Case report

Radiol Iugosl 1990; 24: 171-4

introduction – It has been exactly a hundred years since Billroth in 1889 first described a patient with multilple primary neoplasms (MPN). In 1932, Warren and Gates first reported on a large number of such cases, and proved that cancer patients were at greater risk of developing a second or even a third neoplasm sometime in their life. The authors also set the criteria for MPN diagnosis which have later become generally accepted: 1) each of the tumors must present a definite picture of malignancy; 2) each must be distinct; and 3) the probability that one was a metastatic lesion from the other must be excluded. In studying MPN, Moertel distinguished multiple primary neoplasms according to the site of origin, i.e. those appearing multicentrically in one and the same organ, and others originating in different organs (Table 1). He was convinced that the patients with a particular epithelial neoplasm are at much greater risk of developing a second or even third neplasm ih the same organ or tissue (multiple carcinomas of the aerodigestive and urogenital tracts). As to the appearnce of MPN in different organs, Moertel was, however, sceptical about their presumably greater incidence in cancer patients (1). In 1977; Schoenberg published his findings on the incidence of MPN in Connecticut and Denmark (2) which inequivocally proved that cancer patients were at 31% increased risk of developing another primary malignoma in the same tissue, whereas their risk of developing a second primary malignoma in a different organ was increased by 23%., many studies on MPN in breast cancer patients publiched since the 60's have proved that breast cancer patients run higher risk of developing a second or even third primary malignoma (3, 4, 5, 6, 7, 8), among these ovarian, uterine and colonic carcinomas are believed to be most frequent.

Table 1 – Classification of Multiple Primary Malignant Neoplasms

I.	Multiple primary malignant neoplasms of multicentric origin
	A. The same tissue and organ
	B. A common contiguous tissue shared by different organs
	C. The same tissue in bilaterally paired organs
II.	Multiple primary malignant neoplasms of different tissues or organs
III.	Multiple primary malignant neoplasms of multicentric origin plus a lesion(s) of a different tissue or organ

Received: March 26, 1990 – Accepted: April 2, 1990

Case report – A 71-year old housewife, who had been free of any major health problems so far, noted a lump in her left breast, which proved to be a breast carcinoma on cytology. Based on the clinical status as well as the findings of examinations for evaluating the extent of disease (blood count and chemistry indlucing liver tests, chest X-ray and bone scintiscan) a breast cancer in clinical stage $T_2N_OM_O$ was diagnosed. The patient underwent a modified radical mastectomy. Pathologic examination of breast tissue revealed an invasive ductal carcinoma, G II. The axillary lymph nodes were not involved by carcinoma though all the examined lymph node specimens contained cells of non-Hodgkin lymphoma of KLL type. No adjuvant treatment for breast cancer was indicated. Later on, some additional examinations for staging of NHL were performed. Peripheral lymph nodes were not enlarged, and the remaining clinical findings were within normal limits. On CT of the abdomen, however, enlarged left iliacal lymph nodes were found. Further biopsy of the bone marrow revealed the presence on NHL cells in the bone marrow. The findings of peripheral blood examination were wihtin the limits of normal values. A NHL of KLL type, stage IV A was; diagnosed, which required no treatment. Twenty months later the patient presented with pain in the left shoulder and the left upper extremity. Bone scintiscan revealed a pathologic uptake in the left humerus and the lumbar vertebrae. X-ray of the affected region showed the presence of osteolitic metastases. No metastases in the soft tissue or viseral organs could be established. Hormonal therapy with tamoxifen and irradiation of the left humerus were aplied. This treatment resulted in a partial regression of bone metastases. Three months later the patient presented with massive hematuria. Apart from the enlarged iliac lymph nodes, the abdominal CT performed at that time revealed a tumor in the region of the right kidney, which required nephroureterectomy with lymphadenectomy. On histopathologic examination, the renal tumor was found to be an infiltrative transitional cell carcinoma of the pyelon, G III, whereas the hilar and paraaortic lymph nodes contained NHL infiltrates of KLL type. An additional treatment for this carcinoma was not indicated. During the following two years the patient was receiving continuous hormonal treatment and was subject to regular follow up. The bone metastases were in remission, but enlarged neck and bilateral inguinal lymph nodes appeared. The findings of aspiration biopsy suggested a NHL-KLL type involvement of the lymph nodes, which, however, did not seem to cause any difficulty to the patient; as the findings of blood examinations were all the time within the limits of normal values, no treatment for NHL was considered necessary. In December 1989, i. e. four years after the diagnosis of primary brfeast cancer and NHL, 2 years from the appearance of carcinoma of the right renal pyelon, and 30 month after the confirmation of skeletal metastases, the patient presented with clinically and radiologically evident progress of osteolitic skeletal metastases. CT of the abdomen, performed to explain pain in the lumbar region, showed enlarged iliacal lymph nodes as well as a tumorous mass in the apical part of the left kidney. Angiography of the left kidney imaged an irregular vascularization of the apical part of the left kidney, which was not of hypernephrotic type. Angiographic findings indicated a very high probability of a tumor of the left renal pyelon. Based on the investigations performed so far, in our patient with proven triple malignoma, the appearance of a fourth neoplasm has been suspected, which is most probably another malignoma of multicentric origin in the uropoietic system. Extirpation of the tumor and histologic verification of the process in the left kidney were not indicated because of the patients' advanced age and her poor general condition due to the progress of bone metastases. Encouraged by the favorable effect of first-line hormonal treatment on skeletal metastases, we introduced a second-line hormonal therapy and palliative irradiation for alleviation of skeletal pain as the only treatment.

Discussion – Results of the studies performed on a large number of breast cancer patients during the past few years have confirmed that breast cancer patients are at an increased risk of being affected by other neoplasms as well (6, 7, 8). The largest study carried out in Finland comprised 26 000 patients with breast cancer (Table 2). All the results published so far uniformly confirm the exposure of breast cancer patients to an increased risk of developing a new primary carcinoma in the contralateral breast (1, 2, 3, 6, 7, 8). As to the appearance of new malignomas in other organs, breast cancer patients are believed to be more frequently affected by carcinoma of the genital organs, i. e. ovarian, endometrial and cervical carcinomas (3, 4, 7, 8). The studies analysing the appearance of a secondary malignoma of the genital organs according to the patient's age at breast cancer diagnosis have pointed out that younger women, parti-

Table 2 – Subsequent multiple primary malignant tumors in patients with cancer of the breast (No = 26 617 females) in Finland in 1953-79

Cancer designation	Observed	SIR
Site of first cancer: Breast		
Site or type of new cancer		
Any site (excluding breast)	720	1.17*
Esophagus	16	0.78
Stomach	107	1.11
Colon	62	1.36*
Rectum	33	0.97
Gallbladder, bile ducts	8	0.43*
Lung	46	1.67*
Cervix uteri	33	0.95
Corpus uteri	62	1.33*
Ovary	64	1.73*
Bladder	20	1.65*
Thyroid gland	22	1.95*
Leukemia	36	1.91*

$P < 0.05$
SIR = ratio of observed to expected number of cases

cularly those less than 45 years of age at the time of breast cancer diagnosis, are at greater risk of developing a second malignoma in the ovary (6). A secondary malignoma of the uterus more often appears in women older than 60 years at the time of breast cancer diagnosis (6, 7). Many studies (7, 8) though not all (6) give evidence of an increased risk of breast cancer patients for developing a second primary carcinoma in the colon. Some authors claim that in breast cancer patients the observed morbidity for other neoplasms such as carcinoma of the lung, bladder and thyroid as well as soft tissue sarcomas exceed the expected numbers (7, 8) whereas the reports of other authors do not support this belief (6). The risk of developing a second primary neoplasm increases by observation years. The younger the patient at the time of breast cancer diagnosis is, the greater the risk she runs of developing a new primary carcinoma. The causes for the appearance of multiple primary neoplasms in a person could be ascribed to environmental and genetic factors which are presumably responsible for the rise of multiple neoplasms of different origin. Thus a simultaneous appearance of breast carcinoma and endometrial carcinoma could be ascribed to excessive body weight in these patients as well as to their typical hormonal milieu (9). Familial and hereditary factors are believed to be responsible for a simultaneous rise of breast cancer and ovarian carcinoma, particularly in young patients. As to the frequently reported simultaneous appearance of breast carcinoma and colonic carcinoma, several authors ascribe this phenomenon to particular nutritional habits, as well as to the high socio-economic status of these patients (10).

Considering the differing results and opinions of several prominent authors, it is still questionable whether the observed number of other primary neoplasms in breast cancer patients is actually greater than expected, or it is just a consequence of a more accurate medical follow up of these patients, as it has been presumed by Moertel (1). Also in our patient the second malignoma (NHL of KLL type) was diagnosed on the pathohistologic examination of the lymph nodes removed on surgery for breast cancer. More effective treatment methods result in a prolonged overall survival of cancer patients, and so also of breast cancer patients, which on the other hand represents a greater possibility of appearance and detection of a second or even third neoplasm some time in their life. According to the results of recent studies (6, 7, 8) it can be concluded that at least certain age groups of breast cancer patients are undoubtedly exposed to a greater risk of being affected by particular malignomas. Thus, women with breast cancer have 3–4 times greater possibility of developing another carcinoma in the contralateral breast. Younger breast cancer patients are more frequently affected by ovarian carcinoma, whereas women having breast cancer detected in their older age are more likely to develop endometrial carcinoma. The mentioned correlations are, at presently known facts, the only ones that could justify preventive diagnostic examinations performed in search of a second malignoma. All other possible correlations between breast carcinoma and other neoplasms have not been supported by incontestable and convincing enough evidence so as to allow for any preventive diagnostic measures to be taken in this respect. It is of essential importance, however, that the possibility of a new primary malignoma in breast cancer patients is taken into account, and any possible appearance of new tumorous masses is not automatically regarded as a metastatic spread from breast cancer. Particular attention is required with solitary tumorous lesions in the organs that do not represent a common site of breast cancer metastatic involvement. In such cases histologic verification of the lesions is recommended in individual cases the relevant findings can esentially influence the treatment and prognosis of these patients. Apart from several epidemiologic stu-

dies which prove and confirm an increased risk of MPN in breast cancer patients, the available literature still lacks data on the influence of a second or even third primary malignoma on the treatment and survival of these patients.

Conclusion – In comparison with other women, breast cancer patients are at greater risk of acquiring new primary malignomas some time in their life. In breast cancer patients, the incidence of another primary carcinoma in the contralateral breast is five times greater than in other women. These patients are also more frequently affected by ovarian and endometrial carcinomas. Opinion on other cancer types that are presumed to appear more frequently in breast cancer patients are still differing. It is important, however, that the possibility of second malignoma in breast cancer is taken into account. The appearance of a new tumorous mass must not invariably be interpreted as a metastasis from the primary malignoma. Histologic verification of the tumorous mass can significantly influence the course of treatment and patient's prognosis.

Povzetek

TROJNI KARCINOM PRI BOLNICI S PRIMARNIM KARCINOMOM DOJKE

V članku poročava o bolnici s trojnim malignomom. Ob operaciji primarnega karcinoma dojke je bil s patohistološkim pregledom pazdušnih bezgavk odstranjenih ob operaciji karcinoma dojke ugotovljen ne-Hodgkinov limfom nizke malignostne stopnje v le teh. Nadaljnje klinične, laboratorijske in diagnostične preiskave so pokazale, da ima bolnica poleg karcinoma dojke še ne-Hodgkinov limfom tipa KLL stadij IV A. Dve leti kasneje je bil pri bonici ugotovljen invazivni tranzicicelularni karcilnom pielona desne ledvice. V diskusiji razpravljava o pojavnosti (incidenci) multiplih primarnih neoplazem pri primarnem karcinomu dojke.

References

1. Moertel CG. Multilple primary neoplasma. Historical perspectives. Cancer 1977; 40:1786-1792.
2. Boice JD, Curtis RE, Kleinerman RA, Flannery JT, Fraumeni JF. Summary of multiple primary cancer in Connecticut and Denmark. NCI Monogr 1985; 68:219-292.
3. Schoenberg BS, Greenberg RA, Eisenberg H. Occurence of certain multiple primary cancers in females. J Natl. Cancer Inst 1969; 43: 15-32.
4. Schottenfeld D, Berg J. Incidence of multiple primary cancers. Cancer of the female breast and genital organs. J Natl Cancer Inst 1971; 46:161-170.
5. Weis NS, Daling JR, Chow W H. Incidence of cancer of large bowel in women in relation to reproductive and hormonal factors. J Natl Cancer Inst 1981; 67:57-60.
6. Adami HO, Bergkvist L, Krusemo U, Fersson I. Breast cancer as a risk factor for other primary malignant diseases. A nationwide cohort study. J Natl cancer Inst 1984; 73:1049-1055.
7. Teppo L, Pukkala E, Saxen E. Multiple primary cancer – an epidemiologic exercise in Finland. J Natl Cancer Inst 1985; 75:207-217.
8. Schwartz AG, Ragheb NE, Swanson GM, Satariano WA. Racial and age differences in multiple primary cancer after breast cancer: A population based analysis. Breast Cancer Res Treat 1989; 14:245-254.
9. MacMahon B. Risk factors for endometrial cancer. Gynecol Oncol 1974; 2:122-129.
10. Weiss NS, Daling JR, Chaw WH. Incidence of cancer of the large bowel in women in relation to reproductive and hormonal factors. J Natl Cancer Inst 1981; 67:57-60.

Acknowledgement – The authors thank Dr. Janez Lamovec for the revision of histologic material

Author's Address: Tanja Čufer, MD, The Institute of Oncology, Zaloška 2, 61105 Ljubljana, Yugoslavia