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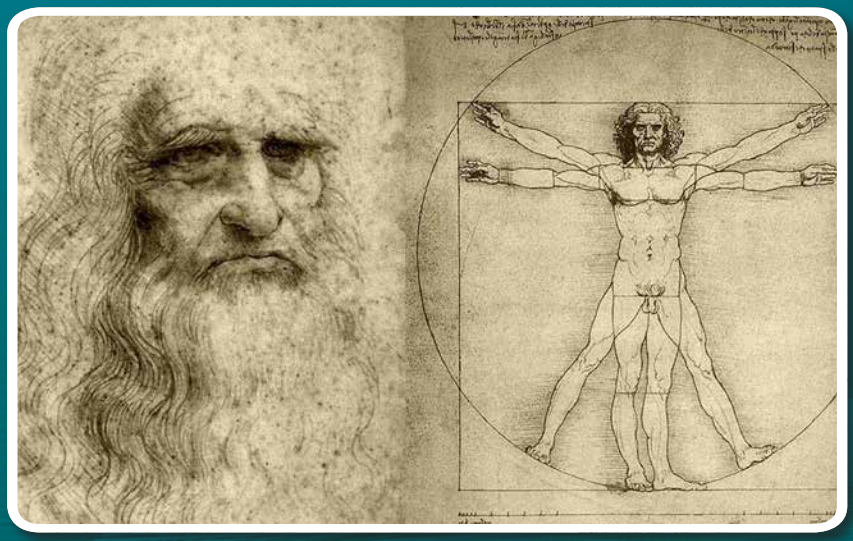

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SECUNDARY MALIGNANT NEOPLASAMS IN PATIENT WITH BREAST CARCINOMA AFTER RADIO AND CHEMOTHERAPY

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СЕКУНДАРНИ МАЛИГНИ НЕОПЛАЗМИ КАЈ ПАЦИЕНТКТА СО КАРЦИНОМ НА ДОЈКА ПО РАДИО И ХЕМОТЕРАПИЈА

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Апстракт

Секундарните малигни неоплазми се канцери предизвикани од третманот со радиотерапија или хемотерапија. Тие не се поврзани со првичниот канцер кој бил третиран и можат да се појават месеци па и години по иницијалниот третман. Со напредокот во дијагнозата и третманот, бројот на излекувани пациенти на долг рок е значително зголемен, но тоа носи зголемена грижа околу ризикот за појава на секундарно индуцирани неоплазми. Во нашиот приказ на случај имаме пациентка која била подложена на радиотерапија и хемотерапија во неколку наврати поради рецидиви на добро диференциран карцином на дојка со карактеристики на цилидром. По 6 години од почетокот на третманот откриен е солиден бубрежен тумор кој подоцна е класифициран како "multilocular renal cell carcinoma", а по 11 години се појавила кожна промена која по екстирпацијата хистопатолошки е класифицирана како дерматофибросарком.

Клучни зборови: секундарни неоплазми, радиотерапија, хемотерапија, карцином

Abstract

Secondary malignant neoplasms (SMN) are cancers caused by treatment with radiotherapy and chemotherapy. They are unrelated to the first cancer that was treated and may occur months or even years after initial treatment. With advances in diagnosis and treatment there is an increasing number of long-term cancer survivors, but also there is growing concern about the risk of radiotherapy and chemotherapy induced malignant neoplasm. In our case report we present a patient that underwent radiotherapy and chemotherapy several times because of recurrence from a well differentiated breast carcinoma with characteristics of cilindroma. After 6 years from the initial treatment a solid renal tumor was found, the histopathological finding from the kidney tissue was "multilocular renal cell carcinoma". After 11 years skin changes appeared, histopathologically classified as dermatofibrosarcomama.

Key words: secondary malignancy, radiotherapy, chemo therapy, cancer

Background

More than half of all the patients with cancer are treated with radiotherapy. With the increasing number of long-term cancer survivors, there is a growing concern about the risk of radiation induced second malignant neoplasm [1,2]. Although radiation exposure is a well-established risk factor for developing SMN, estimation of the true incidence of radiation-induced SMN is difficult . This is due to the fact that, in addition to radiation exposure, the genetic abnormalities (e.g., Li-Fraumeni syndrome) and risk factors associated with primary tumors (e.g., smoking) could predispose the individuals to develop a second cancer [3,4]. Also, changes in chemotherapy protocols have influenced the risk and rate of secondary malignancies in high-risk

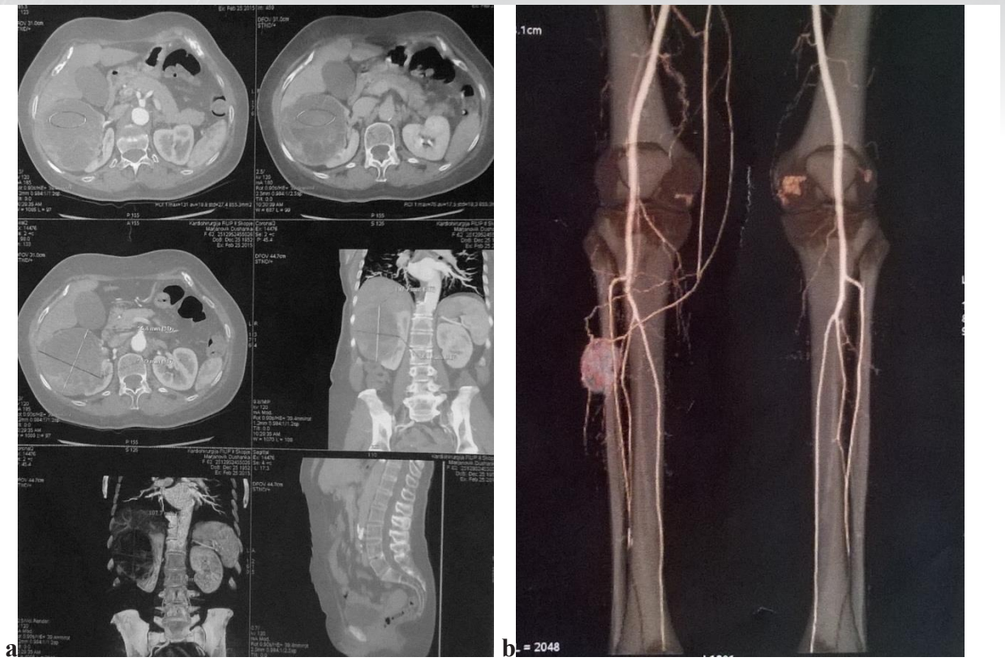

Photo 1. a) *CT of the abdomen showing the large renal tumor before extirpation of the kidney,* ***b)*** *CT angiography of the lower extremities, shows pathological vascularization of the soft tissue lesion which turn out to be dermatofibrosarcoma,* ***c)*** *photo of the skin erosion of the tumor,* ***d)*** *photo of the resected fascia and skin with the tumor - dermatofibrosarcoma.*

populations. The alkylating agents, topoisomerase inhibitors, and anthracycline agents pose the highest risk of initiating carcinogenesis. Normal cells that are especially sensitive to chemotherapy and most likely to begin carcinogenesis include those of the bone marrow, hair follicles, and the epithelial cells of the gastrointestinal tract. Thus, the development of secondary hematologic cancers such as leukemia and lymphoma pose the greatest risk to adult and childhood cancer survivors [5].

Case report

A 46-years-old woman came for check up after noticing 1x1cm nodular change located in the central lobe on her right breast. From the past medical history she gave information that she had been operated from a benign tumor on her left breast nine years ago. Puncture biopsy was made and the result of the microscopic examination was grade I Low-grade (grade 1) cancers are generally the least aggressive and high-grade (grade 4) cancers are generally the most aggressive. The changes on the breast gradually started to increase so, after four months of the first checkup, extirpation was made. The extirpated tissue was histologically examined and morphological characteristics corresponded to well differentiated breast carcinoma with characteristics of cilindroma. The dimensions of the tumor formation were 1,5 x 0,9 x 0,7 cm. Mastectomia totalis sec. Madden was indicated and 17 lymph nodes

were without metastatic deposits. According to this the disease was in the first stadium and the definite histological classification was pTNM = pT1C, G1, pNo, pMx, Co, Eo, Po.

The patient was treated with six cycles of adriamycin and cyclophosphamide (AC) chemotherapy and 50 Gy of local radiotherapy. After four years she had local recurrence in the right infraclavicular region and underwent new surgery and again was treated with radiotherapy. After one year the second recurrence occurred under the right clavicle and around the scar. The whole thoracic wall was exposed to radiotherapy including infra- and supraclavicular regions with 32 Gy in fractions of 4 Gy combined with hypothermia (41 C^0). After one year the third recurrence occurred, followed by resection of the right front wall of the breast including five ribs and part of the distal sternum. Extensive scanning for metastasis was made and solid lesion on the right kidney was found. The dimensions of the lesion ware 95,9 x 110,7 mm (Fig.1a). After eleven years the patient came for checkup after superficial skin injury on the right tibia region on which she had skin changes (Fig.1b,c). Biopsy and extirpation was made and the histology finding was dermatofibrosarkoma. The same year, total right nephrectomy was made and the histologic result from the kidney tissue was "multilocular renal cell carcinoma", classified as pTNM = T2a, Nx Mx, L0, V0, R0.

Discussion

Radiotherapy is a double edged sword. It has a well-established role in the curative treatment of various solid tumors. Unfortunately, radiation has the potential to induce cancer decades after the treatment. This is concerning as there is an increase in the number of long-term cancer survivors. There is an uncertainty in estimating the exact incidence of radiation induced SMN because of the confounding factors such as patient lifestyle and genetic susceptibility. In the meantime, every effort should be made to minimize the influence of factors that could potentially increase the risk of SMN after radiotherapy. A lower total dose of radiation or non-radiation approach could be chosen for treatment whenever evidence supports the benefit without compromising tumor cure [6]. The goal of radiation treatment planning should be to keep the normal tissue exposures to a minimum, more so in pediatric and younger patients. Daily image guidance should be used judiciously to minimize additional cumulative dose at the end of the treatment course. Novel treatment techniques such as the scanned beam proton radiation might decrease normal tissue exposure to leakage neutrons and it also might reduce SMN development [7]. After chemotherapy lifelong surveillance is recommended. Some types of chemotherapy (chemo) drugs have been linked with different kinds of cancer. The cancers most often linked to chemo are myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML). Sometimes, MDS occurs first, and then turns into AML. Acute lymphocytic leukemia (ALL) has also been linked to chemo. Chemo is known to be a greater risk factor than radiation therapy in causing leukemia. [8] Some solid tumor cancers have also been linked to chemo treatment for certain cancers, such as testicular cancer [9].

Conclusion

With recent advances in surgical techniques, chemotherapy, and radiotherapy, there has been a significant increase in the number of long-term cancer survivors. Unfortunately, radiation has the potential to induce cancer decades after the treatment, so every effort should be made to minimize the influence of factors that could potentially increase the risk of secondary malignant neoplasms after radiotherapy

References

1. Ron E. Ionizing radiation and cancer risk: Evidence from epidemiology. Radiat. Res. 1998;150:S30–S41. doi: 10.2307/3579806
2. Howlader N., Noone A.M., Krapcho M., Neyman N., Aminou R., Altekruse S.F., Kosary C.L., Ruhl J., Tatalovich Z., Cho H., et al.SEER Cancer Statistics Review, 1975–2009. National Cancer Institute; Bethesda, MD, USA: 2012
3. Li F.P., Fraumeni J.F. Soft-tissue sarcomas, breast cancer, and other neoplasms. A familial syndrome? Ann. Intern. Med. 1969;71:747–752
4. Sasco A.J., Secretan M.B., Straif K. Tobacco smoking and cancer: A brief review of recent epidemiological evidence. Lung Cancer. 2004;Suppl. 45:S3–S9.

Vega-Stromberg, Teri MSN, RN, AOCN. Journal of Infusion Nursing: November/December 2003 - Volume 26 - Issue 6 - pp 353-361

Kumar, S. Second Malignant Neoplasms Following Radiotherapy. *Int. J. Environ. Res. Public Health* 2012, 9, 4744-4759.

5. Travis L.B., Ng A.K., Allan J.M., Pui C.H., Kennedy A.R., Xu X.G., Purdy J.A., Applegate K., Yahalom J., Constine L.S., et al. Second malignant neoplasms and cardiovascular disease following radiotherapy. J. Nat. Cancer Inst. 2012; 104:357–370.
6. N Hijiya, MM Hudson, S Lensing , etal: Cumulative incidence of secondary neoplasms as a first event after childhood acute lymphoblastic leukemia JAMA 297: 1207– 1215,2007
7. Fung C., Fossa S.D., Beard C.J., Travis L.B. Second malignant neoplasms in testicular cancer survivors. J. Natl. Compr. Canc. Netw. 2012;10:545–556

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