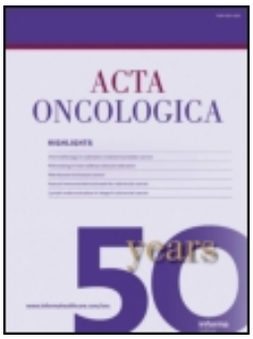

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: informahealthcare.com/journals/ionc20

Triple malignancy: Sequential development of second and third primary tumors in a patient with Hodgkin's lymphoma

George A. Giannopoulos, George H. Sakorafas, Aikaterini Parasi, Nikolaos Tzanakis, George Ralis & George Peros

To cite this article: George A. Giannopoulos, George H. Sakorafas, Aikaterini Parasi, Nikolaos Tzanakis, George Ralis & George Peros (2007) Triple malignancy: Sequential development of second and third primary tumors in a patient with Hodgkin's lymphoma, Acta Oncologica, 46:8, 1187-1189, DOI: 10.1080/02841860701367852

To link to this article: https://doi.org/10.1080/02841860701367852

Published online: 08 Jul 2009.

Acta Oncologica, 2007; 46: 1187–1189

informa
healthcare

LETTER TO THE EDITOR

Triple malignancy: Sequential development of second and third primary tumors in a patient with Hodgkin's lymphoma

GEORGE A. GIANNOPOULOS[1], GEORGE H. SAKORAFAS[1], AIKATERINI PARASI[1], NIKOLAOS TZANAKIS[1], GEORGE RALIS[1] & GEORGE PEROS[1]

[1]*4th Department of Surgery, Athens University, Medical School, Attikon University Hospital, Athens, Greece*

To the Editor

A 30-year-old patient was presented to our hospital complaining of easy fatigue, tiredness, epigastric pain after the ingestion of food and radiated to the right hypochodrium. He also reported melena three days before his admission. When he was 13-years-old he was diagnosed with Hodgkin's lymphoma at the left cervical area (stage IA). He was treated by radiation therapy (40 Gy in total, one month duration). As usual at that time, he also underwent splenectomy as a staging procedure [4]. His family history was free; he was neither a smoker nor a regular alcohol or drug user. Clinical examination showed the manifestations of anemia (on inspection) and the presence of melena during the digital examination of the rectum. Laboratory investigation showed anemia (Hct = 20.9%, Hb: 6.9 g/dl, MCV: 87.2 fl) and was otherwise negative. Upper gastrointestinal endoscopy revealed an intraluminal ulcerated mass in the area of the cardioesophageal junction. Endoscopic biopsies were positive for malignancy (sarcoma). Colonoscopy was without pathologic findings. Abdominal computed tomography showed a solid mass of soft tissue density at the area of the gastroesophageal junction with morphological characters of malignant tumor. A slight enlargement of regional lymph nodes was also imaged. The patient underwent total gastrectomy. Postoperative course was uneventful and the patient was discharged on postoperative day 13. Histology revealed a large ($6 \times 3.5 \times 2$ cm) sarcoma, with extensive ulceration of the mucosa. The tumor infiltrated the local fatty tissue. Immunohistochemistry confirmed the diagnosis of a sarcoma (positive to vimentin and desmin, and – to a lesser extent – to smooth muscle actine and to protein NSE and negative to CD34 as well as to C-kit). Thus, the final diagnosis was of a Grade 2 (according to Costa) T3N0 sarcoma of the gastric cardia.

Twenty months later the patient was again admitted to our department complaining of weight loss ($\sim$10 kg), observed during the last 6 months. He also noted a palpable lesion behind the nipple of the right breast. Clinical examination revealed a painless, hard and mobile mass behind the nipple of the right breast and lymphadenopathy at the right axilla. As reported in the medical records, clinical examination of the breasts was negative during the previous admission of the patient. Laboratory investigation was without pathologic findings (except of slight leucocytosis, as expected due to previous splenectomy). Recurrence of the sarcoma was excluded at that time by upper gastrointestinal endoscopy and abdominal computed tomography which were negative. Computed tomography of the thorax showed the palpable breast lesion, but was otherwise negative. Fine needle aspiration biopsy of the breast lesion revealed a breast carcinoma. The patient underwent a modified radical mastectomy of the right breast. Postoperative course was uneventful and the patient was discharged on postoperative day 4. Histology revealed a ductal invasive carcinoma of the breast (maximum diameter of 2.5 cm, Grade 3),

Correspondence: George H. Sakorafas, Arkadias 19–21, GR-115 26, Athens, Greece. Tel +30 210 74 87 318. Fax +30 210 74 87 192. E-mail: georgesakorafas@yahoo.com

(Received 5 January 2007; accepted 27 March 2007)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.1080/02841860701367852

infiltrating the nipple, with the presence of many neoplastic emboli within lymph vessels and with metastases in three of the 14 resected axillary lymph nodes. The tumor was ER and PR positive (90% and 60%, respectively), Ki 67 (+), c-erbB-2 (+), BCL-2 (+) and p53 (−). The patient received adjuvant chemotherapy and hormonotherapy.

Twenty seven months following gastrectomy a recurrence of the sarcoma was diagnosed, and the patient died from generalized disease, about 38 months after gastric surgery.

Current therapeutic methods can achieve high (>85%) cure rates in patients with Hodgkin's lymphoma [1–3]. However, these therapeutic regimens (which include radiotherapy and chemotherapy) have been associated with an increased incidence of a late side effect, the development of other primary metachronous tumors. These tumors represent a major cause of mortality in patients with Hodgkin's lymphoma after the cure of their disease [4]. Most commonly, these metachronous neoplasms include solid tumors (which can be observed almost anywhere, i.e. in the lungs, gastrointestinal tract, blood system, breast, prostate, female reproductive system, thyroid, and skin), as well as blood malignancy (usually acute leukemia) [5–13]. Typically, these metachronous tumors are diagnosed after more than 15 years following treatment of Hodgkin's lymphoma [14]. Blood malignancies are less common in total, but are more frequently observed during the first decade after treatment of Hodgkin's lymphoma [3].

The increased risk for the development of second or even third primary malignancy in these patients is probably due to the therapeutic treatment of Hodgkin's lymphoma. Radiation therapy techniques (in particular the high doses used during the past decades, as well as the extended field of irradiation) have been implicated for the development of breast and thyroid cancer. Alkylating agents-based chemotherapy may be implicated in the development of blood malignancies during the first decade following treatment and of solid tumors after 15 years [3]. Moreover, splenectomy, which was used in the past as a staging procedure (as in our patient), may predispose to the development of other second primary tumors [15,16]; however, this is a controversial issue [1].

To reduce the risk of metachronous primary tumor(-s) development in patients treated for Hodgkin's lymphoma a variety of modified therapeutic manipulations have been proposed, including the use of lower radiation doses, narrow radiation fields, combination therapy (radiation therapy and chemotherapy), prophylactic use of tamoxifen in women with other risk factors for breast cancer, etc [1,14,17,18]. Due to the high risk for metachronous primary tumor development, patients treated for Hodgkin's lymphoma should be followed for a long period (even up to 20 years). In addition to the usual clinical and laboratory investigation, whole body CT scan and PET scan have been proposed for the follow-up of these patients [3]. The identification of molecular indices that could be used to detect the increased risk for second primary malignancy has been proposed to identify patients at the highest risk. This approach is theoretically very appealing, since it will allow the determination of the highest risk group, which should be followed much more closely, with a more intensive follow-up program.

References

[1] Deniz K, O'Mahony S, Ross G, Purushotham A. Breast cancer in women after treatment for Hodgkin's disease. Lancet Oncol 2003;4:207–14.

[2] Wolden SL, Hancock SL, Carlson RW, et al. Management of breast cancer after Hodgkin's disease. J Clin Oncol 2000;18: 765–72.

[3] Ng A, Bernardo P, Weller E, et al. Second malignancy after Hodgkin disease treated with radiation therapy with or without chemotherapy: Long-term risks and risk factors. Blood 2002;100:1989–96.

[4] Lee CK, Aeppli D, Nierengarten ME. The need for long-term surveillance for patients treated with curative radiotherapy for Hodgkin's disease: University of Minnesota experience. Int J Radiat Oncol Biol Phys 2000;48:169–79.

[5] van Leeuwen FE, Chorus AM, van den Belt-Dusebout AW, et al. Leukemia risk following Hodgkin's disease: Relation to cumulative dose of alkylating agents, treatment with teniposide combinations, number of episodes of chemotherapy, and bone marrow damage. J Clin Oncol 1994;12:1063–73.

[6] Biti G, Cellai E, Magrini SM, Papi MG, Ponticelli P, Boddi V. Second solid tumors and leukaemia after treatment for Hodgkin's disease: An analysis of 1121 patients from a single institution. Int J Radiat Oncol Biol Phys 1994;29:25–31.

[7] Boivin JF, Hutchison GB, Zauber AG, et al. Incidence of second cancers in patients treated for Hodgkin's disease. J Natl Cancer Inst 1995;87:732–41.

[8] Doria R, Holford T, Farber LR, Prosnitz LR, Cooper DL. Second solid malignancies after combined modality therapy for Hodgkin's disease. J Clin Oncol 1995;13:2016–22.

[9] Salloum E, Doria R, Schubert W, et al. Second solid tumors in patients with Hodgkin's disease cured after radiation or chemotherapy plus adjuvant low-dose radiation. J Clin Oncol 1996;14:2435–43.

[10] Maurizi Enrici R, Anselmo AP, Osti MF, et al. Analysis of the risk of solid tumor following Hodgkin's disease. Haematologica 1997;82:57–63.

[11] Swerdlow AJ, Barber JA, Hudson GV, et al. Risk of second malignancy after Hodgkin's disease in a collaborative British cohort: The relation to age at treatment. J Clin Oncol 2000; 18:498–509.

[12] van Leeuwen FE, Klokman WJ, Veer MB, et al. Long-term risk of second malignancy in survivors of Hodgkin's disease treated during adolescence or young adulthood. J Clin Oncol 2000;18:487–97.

[13] Cellai E, Magrini SM, Masala G, et al. The risk of second malignant tumors and its consequences for the overall

survival of Hodgkin's disease patients and for the choice of their treatment at presentation: Analysis of a series of 1524 cases consecutively treated at the Florence University Hospital. Int J Radiat Oncol Biol Phys 2001;49:1327–37.

[14] Dores G, Metayer C, Curtis E, et al. Second malignant neoplasms among long-term survivors of Hodgkin's disease: A population-based evaluation over 25 years. J Clin Oncol 2002;20:3484–94.

[15] Dietrich PY, Henry-Amar M, Cosset JM, Bodis S, Bosq J, Hayat M. Second primary cancers in patients continuously disease-free from Hodgkin's disease: A protective role for the spleen? Blood 1994;84:1209–15.

[16] Munker R, Grutzner S, Hiller E, et al. Second malignancies after Hodgkin's disease: The Munich experience. Ann Hematol 1999;78:544–54.

[17] Chung CT, Bogart JA, Adams JF, et al. Increased risk of breast cancer in splenectomized patients undergoing radiation therapy for Hodgkin's disease. Int J Radiat Oncol Biol Phys 1997;37:405–9.

[18] Abrahamsen A, Andersen A, Nome O, Jacobsen A, Holte H, Abrahamsen J, et al. Long-term risk of second malignancy after treatment of Hodgkin's disease: The influence of treatment, age and follow-up time. Ann Oncol 2002;13: 1786–91.