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LETTER TO THE EDITOR

Radiation-induced oesophageal carcinoma after breast carcinoma: A report of five cases including three successfully treated by radiochemotherapy

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To the Editor

The carcinogenic effect of radiation therapy is well described and several cases of oesophageal cancer after radiation for breast, head and neck, or lung cancer have been reported. Women given radiation therapy for breast cancer have an increased risk of developing lung carcinoma or sarcoma [1–4]. A retrospective analysis of more than 220 000 patients treated for breast cancer enabled an estimate of the increased relative risk of oesophageal cancer after radiation of the internal mammary nodes [5]. We report here the cases of five patients who recently developed oesophageal cancer several years after receiving radiation therapy for breast cancer.

Patient number 1

A 52-year-old woman with no history of alcohol consumption or cigarette smoking underwent mastectomy and axillary dissection in 1980 for breast carcinoma (pT2c N1b M0). She was given radiation therapy (45 Gy to the thoracic wall, the axillary and supraclavicular nodes and 50 Gy to the internal mammary nodes), followed by 12 chemotherapy sessions (CMF). In June 2000, she consulted for dysphagia. Oesophagoscopy demonstrated an ulcerated stricture in the middle third of the oesophagus. Biopsies confirmed a poorly differentiated squamous-cell carcinoma (SCC). CT scan staging was

T3N1M0. This tumour had developed in the field of radiation delivered to the internal mammary nodes: 16 to 20 Gy had been delivered to the oesophagus. A new radiation protocol was considered feasible. She was thus given concomitant radiochemotherapy with chemotherapy (5FU and CDDP). Because of poor clinical tolerance, 5-FU was removed and CDDP was delivered in combination with radiation (60 Gy in 30 sessions from July to August 2000). Endoscopic control with biopsies CT scan were normal one month after the end of treatment confirming complete response. The patient 5 years after the end of treatment is still in complete clinical and endoscopic response without any clinically detectable anomaly of the oesophageal motricity despite a cumulative radiation dose of nearly 80 Gy.

Patient number 2

A 74-year-old patient with no history of alcohol consumption or smoking was admitted to our centre in 2002 with a pleural recurrence of a mixed SCC and glandular carcinoma of the lower third of the oesophagus. She was treated 2 years earlier by surgery; the pathology examination of the surgical specimen staged the tumour T3N0 with a very intense fibrosclerous reaction. This patient had been given exclusive “very high dose” radiation therapy in 1974 for a small cancer of the left breast:

83–87 Gy to the tumour site, 75 Gy to the axillary nodes, 56 Gy to the supraclavicular nodes, and 62 Gy to the internal mammary nodes. She had severe radiation sequelae: sclerotic skin reactions, modifications of the left hemisternum, radiation-induced plexitis with paralysis of the left arm, and vesiculopapillary cancer of the thyroid in 1987 (treated by thyroidectomy and radioactive iodine). In 1997, she developed a cancer of the right breast treated by tumorectomy and “classical” external radiotherapy without radiation of the internal mammary nodes. Recurrence of the oesophageal cancer was treated by chemotherapy (5FU-CDDP) which was rapidly interrupted; the patient died a few weeks later, i.e. 30 months after surgery.

Patient number 3

A 48-year-old woman with a long history of cigarette smoking (15 package-years) and moderate alcohol consumption (20 g/d) was admitted with a diagnosis of SCC of the oesophagus. She had been treated in 1990 for cancer of the right breast. Tumorectomy was followed by radiation therapy (45 Gy to the breast, the axillary nodes, the supraclavicular nodes, and the internal mammary nodes with a supplementary dose of 14.4 Gy delivered to the tumourectomy site) and four chemotherapy sessions (FEC 50). In 2002, she developed dysphagia leading to the diagnosis of SCC of the lower third of the oesophagus. The CT staging was T3N1M0. The dosimetric file showed that the oesophageal tumour developed at the lower limit of the radiation field of the internal mammary nodes, area which had received an estimated dose of 16–20 Gy. She was treated by concomitant radiation (50 Gy in 25 sessions over 5 weeks) and chemotherapy (4 sessions of 5FU-CDDP). Post-treatment endoscopy and CT demonstrated complete local and nodal response. Complete response persisted at last follow-up, 5 years after diagnosis.

Patient number 4

A 74-year-old woman, with no history of smoking or alcohol consumption, presented weight loss, iron-deficiency anaemia and retrosternal pain. Explorations revealed SCC of the mid and lower thirds of the oesophagus with multiple hepatic metastases. The patient had a long history of breast cancer. In 1975 she had undergone tumourectomy and radiotherapy for cancer of the right breast and, in 1985, the same treatment for cancer of the left breast, followed by chemotherapy, then in 1995 surgery and radiotherapy for local recurrence. The radiation fields and doses were not available, but in 1985

radiation had been complicated by clinical signs of oesophagitis. Three sessions of chemotherapy were delivered but she died shortly thereafter, i.e. 3 months after the initial diagnosis.

Patient number 5

A 62-year-old woman, who had never smoked nor drunk alcohol, presented in January 2005 retrosternal pains and a mild dysphagia. Endoscopy revealed a large esophageal ulcer located in the upper third; and biopsies demonstrated a SCC; on CT scan the tumour was classified as T3N1M0. She was treated in 1991 for a cancer of the left breast by resection and radiotherapy: 45 Gy to the thoracic wall, the axillary nodes and 45 Gy to the internal mammary nodes. She had no esophageal symptom during this treatment. The dosimetric file showed that the oesophageal tumour developed in the radiation field of the internal mammary nodes, and had received an estimated dose of 20 Gy. She was treated by concomitant irradiation (54 Gy) with four cycles of LV5FU-CDDP (50 mg/m² of CDDP every 2 weeks). Endoscopic control 2 months after the treatment revealed a benign stenosis of the upper oesophagus. Endoscopic dilation was done in June 2006. In December 2006, 2 years after the diagnosis, she has a moderate dysphagia, related to a mild benign stricture.

Discussion

These five cases illustrate that radiation of the mediastinum for breast cancer, increases the risk of radiation-induced oesophageal cancer which can nevertheless respond to radiation at classical doses. Between January 1988 and December 2005, 169 women were treated for oesophageal cancer in our centre. Five (3%) had a history of mediastinal radiation for breast cancer delivered several years earlier. There are several arguments suggesting these cancers were radiation-induced. First, the known risk factors of alcohol consumption and cigarette smoking were absent in four of the five patients. All patients had criteria of radiation-induced cancer: a) history of radiation; b) cancer occurring in the prior field of radiation; c) latency period of several years between radiation and diagnosis of cancer; d) presence of radiation-induced lesions in neighbouring tissues (patient no. 2) [2–4]. Radiation therapy for breast cancer is a recognized risk factor for oesophageal cancer. In a retrospective study of 220 806 women followed for breast cancer between 1973 and 1993, Ahsan and Neugut [5] reported 116 cases of oesophageal cancer for an expected 75.5 (relative risk 1.54). This risk increased with time in

the radiated population: more than 10 years after radiation, the relative risk of oesophageal cancer was 5.42 for SCC and 4.22 for adenocarcinoma. In a second cohort of more than 60 000 patients who had undergone surgery for breast cancer with or without radiation therapy, the relative risk of oesophageal cancer 15 years after radiation was 2.19 in the radiated patients [6]. The majority of radiation-induced cancers of the oesophagus are squamous-cell carcinomas.

Different treatments have been proposed for these patients with a history of radiation. Surgery is preferred by most authors [4,7]. Radiation therapy is rarely proposed despite the absence of major complications in the few cases reported in the literature [7]. In our three patients, the oesophagus had received an estimated dose of 16 to 20 Gy during the radiation of the internal mammary nodes. The oesophageal tumour was situated either in the radiation field of the internal mammary nodes or at its lower limit. The dosimetry allowed a second radiation protocol of 50–60 Gy. Surprisingly, we did not observe any radiation-related acute adverse effects or functional sequelae (no clinically detectable oesophageal motricity disorder), and our three patients given radiation therapy are still alive with complete response.

In conclusion, the development of oesophageal cancer in women who have a history of adjuvant radiation of the internal mammary nodes for breast cancer is not exceptional [8]. Our cases occurred recently (2000–2005): should new cases be expected

since modern techniques are less likely to include the internal mammary nodes (and thus the oesophagus) in the radiation field? It must be noted that a history of radiation therapy does not contraindicate a new radiation protocol in combination with chemotherapy, particularly if the second radiation is delivered many years after the first.

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