

SHORT COMMUNICATIONS AND CASE REPORTS

Synchronous appearance of male breast cancer and pancreatic cancer 15 years after the diagnosis of testicular cancer - report of a case

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Summary

The frequency of new neoplastic diseases among patients cured of testicular cancer is higher than in normal population. For these patients, synchronous occurrence of multiple neoplasms is not common. Also, less than 1% of all cases of breast cancer occur in males. We present herein a case having both breast and concurrent pancreatic cancer after being effectively treated for testicular cancer. To the best

of our knowledge, this is the first case of synchronous breast and pancreatic cancer in a male patient following testicular cancer. Second cancer is the most severe long-term complication of chemotherapy or radiotherapy for patients with testicular cancer and the possibility of multiple cancers has to be taken into consideration when multiple lesions are present.

Keywords: male breast cancer, multiple primary carcinomas, pancreatic cancer, testicular cancer

Introduction

Second primary cancers represent the most severe long-term complications of chemotherapy or radiotherapy for patients cured of their primary malignancy [1]. Testicular cancer survivors are at statistically significantly increased risk of solid tumors for at least 35 years after the initial diagnosis [1-6].

There have been several reports on the increased risk for a variety of cancers following testicular cancer but description of male breast cancer following testicular cancer has been extremely rare [2].

Breast cancer is seen infrequently in men. Less than 1% of all cases of breast cancer occur in males [7]. In this report we present a male patient who developed synchronous breast cancer and pancreatic cancer 15 years after initial treatment of testicular cancer. Clustering of three malignancies in a single patient is a rare occurrence, and, to our knowledge, this is the first report this combination of two synchronous cancers appearing

in a patient with a history of testicular cancer. Second cancers are a real hazard following treatment of testicular cancer and should always be considered during long-term follow-up in order to detect them early for possible curative treatment [2].

Case presentation

A 50-year-old man who had previously undergone right-sided orchiectomy and chemotherapy (8 cycles with cisplatin, bleomycin and vincristine) for mixed germ cell testicular tumor 15 years ago was admitted to our hospital complaining of retraction in his right nipple and abdominal pain. His father had died of lung cancer, and both of his sisters had also a history of breast cancer. On physical examination of the breast, right nipple retraction was detected without any palpable mass and axillary lymph nodes. Physical examination revealed an absent right testis and a normal left one. Upon mam-

mographic examination and breast ultrasonography, a solid lesion measuring 13×11 mm in the right breast and reactive axillary lymph nodes were detected (Figure 1a, 1b). Abdominal magnetic resonance imaging (MRI) revealed a 2.5×2.5 cm mass in the head of pancreas (Figure 2). Positron emission tomography (PET) showed a high uptake of fluoro-2-deoxy-D-glucose in regions corresponding to the head of the pancreas and right nipple. CA 19.9 level was elevated at 3584 U/ml (normal range 3-33), whereas serum β -human chorionic gonadotropin (β -hCG) and alpha-fetoprotein (AFP) levels were normal. Whipple operation and right-sided simple mastectomy were carried out in a single session. Histological examination revealed the tumor in the head of the pancreas to be adenocarcinoma (Figure 3). There were 2 metastatic peripancreatic lymph nodes; estrogen and progesterone receptors were negative. Pathological examination of the resected material of simple mastectomy was consistent with invasive ductal carcinoma (Figure 4a). The tumor was grade I and its size was 1.1×0.8 cm. Lymphatic vessels were invaded while lymph nodes were not sampled. Estrogen receptors were focally positive and progesterone receptors were negative (Figure 4b). C-erb-B2 was negative. The skin and the nipple were invaded, and the surgical margins were negative. The patient underwent radiotherapy to the pancreatic region and also to the chest wall. Chemotherapy consisting of 5-fluorouracil and gemcitabine was administered every 2 weeks [8]. After 6 cycles of chemotherapy, the patient underwent a thoracic and abdominal computerized tomography. The imaging procedures revealed multiple metastatic lesions in both lungs and liver, multiple intraabdominal lymphadenopathy and metastatic changes of bones. The patient refused further treatment and died 10 months after the diagnosis.

Discussion

The frequency of neoplastic diseases among patients cured of testicular cancer is higher than in normal population [1-6]. The relative risk for the development of second cancers in patients treated for testicular cancer is 1.65 [1-3]. Significantly elevated relative risks were found for leukemia, melanoma, sarcoma, cancers of the lung, colon, rectum, pancreas, stomach, prostate, bladder, kidney and contralateral testis [1-6]. Increased incidence was also suggested for cancer of the pleura and esophagus [2].

Travis et al. [2] identified 40,576 patients with testicular cancer and reported a total of 2,285 second solid cancers among them. Only 3 patients with breast cancer were reported. It is known that the risk of pan-

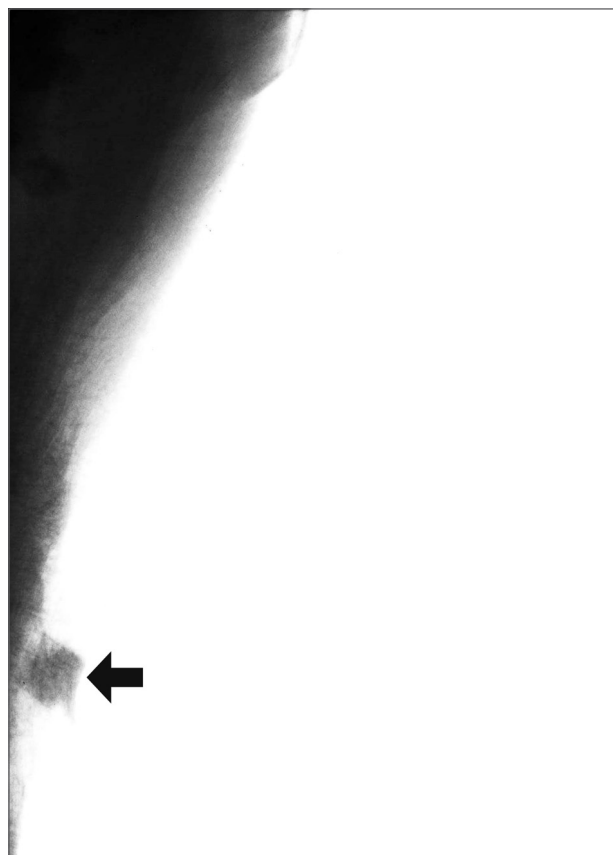


Figure 1a. Mammography shows a 13×11 mm solid lesion in the right breast (arrow).

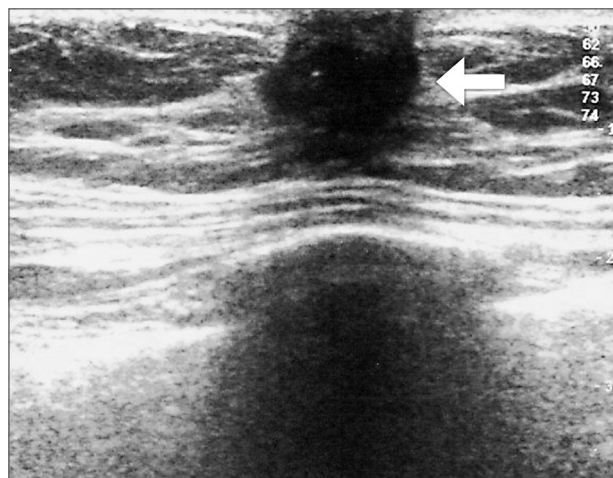


Figure 1b. Breast ultrasonography shows a hypoechoic solid lesion with skin invasion (arrow).

creatic cancer is increased in testicular cancer but breast cancer observed as second cancer is very rare [2].

The highest risk for secondary neoplasm following treatment of testicular cancer is associated with the use of radiotherapy. No significantly elevated risk for



Figure 2. Fat saturated, contrast enhanced, T1 weighted transverse images of MRI reveal a mass (2.5×2.5 cm) in the head of pancreas (arrow).

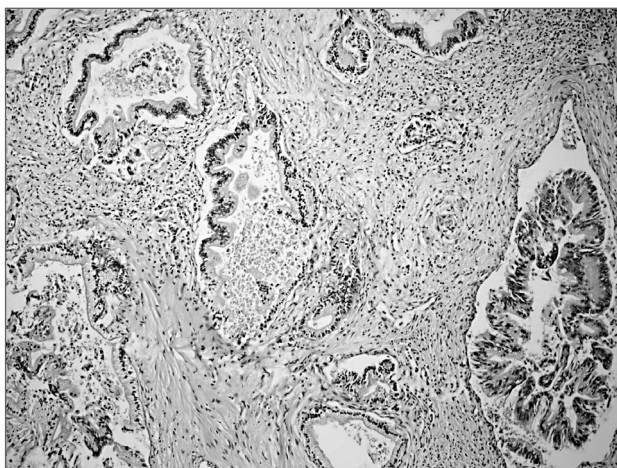


Figure 3. Adenocarcinoma forming ductal structures in pancreatic tissue (H&E ×100).

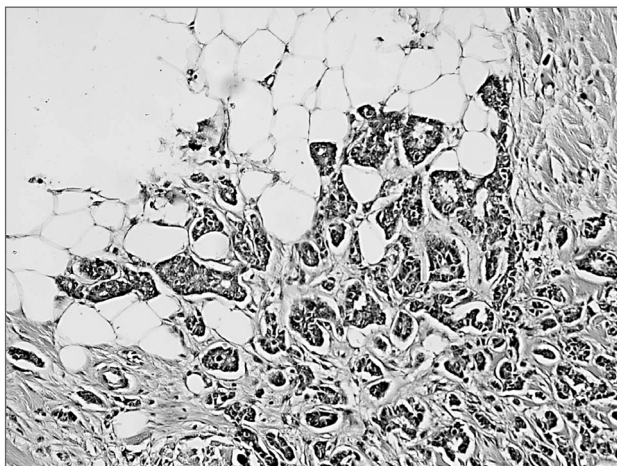


Figure 4a. Infiltrative carcinoma forming ductal structures in breast tissue (H&E ×40).

secondary solid tumors was observed after treatment with chemotherapy alone [1,3-6]. However, the role of chemotherapy for testicular cancer in the development of second solid tumors has been analyzed only in small series of patients with relatively short follow-up period. So, no definitive association between chemotherapy and risk of second cancers could be established [1-3]. Recently, Travis et al. [2] conducted a study in which they quantified the long-term site-specific absolute and relative risks of incident solid cancers among more than 40,000 1-year survivors of testicular cancer. In that study, it was reported that treatment of testicular cancer with chemotherapy alone was associated with statistically significantly increased risk of solid cancers, but analytic studies will be required to quantify treatment-specific risks and determine their causes [2]. The majority of patients with testicular cancer are cured by cisplatin-based chemotherapy. Platinum is retained in the human body long after the completion of treatment [9,10]. In animal models, platinum has been reported to cause solid tumors, as well as leukemia. Cisplatin has been recognized as a possible human carcinogen [11]. Whether chronically raised platinum concentrations have an influence on the development of secondary malignancies is not known [9,10]. Major endocrinological abnormalities were identified in more than half of chemotherapy-treated, long-term survivors of testicular cancer [12]. Impairment of Leydig cell function and low testosterone levels were reported in chemotherapy-treated testicular cancer patients [13,14].

The etiology of male breast cancer is poorly understood. Hormonal alterations due to testicular disease may be an important factor. Also, males with testicular injury are at increased risk of breast cancer, perhaps due

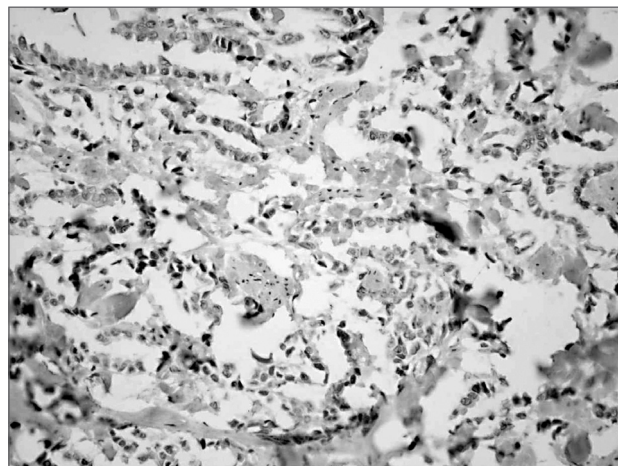


Figure 4b. Immunohistochemical staining demonstrates nuclear ER positivity in tumor cells (×200).

to androgen deficiency or excess estrogens [7]. Testosterone deficiency found in chemotherapy-treated patients with testicular cancer might have occurred in our patient and this hormonal alteration might also have contributed to development of breast cancer.

Our patient received chemotherapy alone after orchiectomy. Second solid cancers related to radiotherapy and chemotherapy occur much later than leukemias [1,5] and the cancers of our patient occurred in the second decade after the treatment of his first cancer. So, from the chronological point of view, they can be attributed to chemotherapy. Otherwise, it can be a simple coincidence.

Other etiological factors for breast cancer include trauma, smoking, and history of rapid weight gain. A family history of breast cancer, in man or woman, is certainly a risk factor [7]. Sisters and daughters of male breast cancer patients have a 2- to 3-fold increased risk of developing breast cancer. The risk of breast cancer is significantly increased in males with a history of breast cancer in first-degree relatives [7].

The development of breast cancer in our patient may be related with chemotherapy. But factors unrelated to treatment –possibly genetic predisposition– should also be considered in our patient. An individual developing more than one primary tumor in anatomically and functionally unrelated organs may be considered as cancer-prone [15]. People with a family history of cancer will inherit genetic cancer susceptibility as a risk factor for cancer [15]. In our patient there was a family history of cancer. His two sisters had breast carcinoma and his father had died of lung cancer. Thus, we think that one of the roles for such concurrent neoplasms in this patient belongs to genetic predisposition. Unfortunately, we could not perform a genetic analysis in our patient due to his refusal. Additionally, our patient was a heavy smoker which is known as an etiological factor for breast and pancreatic cancer.

In the evaluation of our patient, single pathological examination only from one of these two lesions (breast and pancreas) could lead to incomplete diagnosis. The pathological examination of both of the lesions in the breast and in the head of pancreas were performed and two different neoplasms were found. So, a biopsy of a second separate lesion which is not evidently a metastasis can show a different tumor with different therapeutic strategy and prognosis. Multiple cancers have to be suspected in patients with increased risk for malignancies. The above reported patient with synchronous pancreatic and breast cancer is an example of a patient with risk factors such as breast cancer in first degree relatives and history of chemotherapy for a previous cancer.

In conclusion, clinicians should be alert for the ap-

pearance of another tumor in cancer patients. It could be either metastasis or another malignancy. The possible risk of multiple primary neoplasms should be taken into consideration in patients with testicular cancer. Chemotherapy-treated survivors of testicular cancer should be monitored for late toxicity throughout their lives [2]. In addition, the combination of the three different neoplasms (mixed germ cell testicular tumor, male breast cancer and pancreatic cancer) in one patient, to the best of our knowledge, has not been reported before.

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