Case report

COMPLETE RESPONSE IN SYNCHRONOUS EARLY BREAST AND LUNG CANCER

Mariela Vasileva-Slaveva¹, Alexandrina Vlahova², Spartak Valev³, Assia Konsoulova⁴, Svilen Masliankov¹
1) Department of Surgery, Alexandrovska University Hospital, Sofia, Bulgaria.
2) Department of Pathology, Alexandrovska University Hospital, Sofia, Bulgaria.
3) Department of medical oncology, MBAL “Nadezhda”, Sofia, Bulgaria.
4) Department of medical oncology, Complex Oncological center Burgas, Bulgaria.

SUMMARY
This is a rare case of multiple primary malignancies (MPM) both diagnosed in early stage, for which the patient received multidisciplinary complex treatment and achieved no evidence of disease state. We present a 67-year-old woman admitted in the Department of General surgery, Alexandrovska University Hospital, in April 2017 and diagnosed with invasive ductal carcinoma in the inner lower quadrant of the right breast. During the detailed staging process was found also 2 cm adenocarcinoma in the left lung. The patient underwent upper left lobectomy as a single treatment for lung cancer and received neoadjuvant chemotherapy with Docetaxel, Trastuzumab, and Pertuzumab for breast cancer. After the performed breast-conserving surgery, the final pathological report showed pathologic complete response (pCR). The current treatment modalities provide prolongation of patients’ life, which will increase the rate of MPM. Excellent prognosis still can be achieved when the right management of the patient is applied.

Keywords: multiple primary malignances, breast cancer, pathologic complete response,

BACKGROUND
Multiple primary malignancies (MPM) are defined by the presence of at least two independent primary malignancies in the same or different organs of a single patient. [1] The new incidence rate of the MPM varies between 2.4% and 8%, up to 17% within 20 years of follow-up. [2] MPM can be synchronous (various definitions: occurring at the same time or within 2-month [3] or 6-month [2]) or metachronous (developed at more than a 2-month [3] or 6-month [2] interval, respectively). Detection of MPM is becoming more frequent with developing diagnostics and prolongation of life and, as in this case, increasing the incidence rate in Bulgaria of both breast and lung cancer in women. [4]

CASE DESCRIPTION
This is a case of 67-year old woman, presented in Department of General surgery, Alexandrovska University Hospital, in April 2017 with 2 cm formation in the inner lower quadrant of the right breast. The patient had well-controlled arterial hypertension and no family history of cancer. She was a smoker – one pack of cigarettes per day for 40 years.

The mammography showed a lesion with an irregular shape, measuring 27 mm; no microcalcifications and no suspicious lymph nodes in the right axilla, BIRAD score 4. The ultrasound examination confirmed the mammographic findings. The laboratory tests were in the normal range, including Ca 15-3 (14.63 U/ml). We performed a core needle biopsy, which revealed poorly differentiated invasive ductal breast cancer (Fig. 1.), G3, ER-positive (8 points), PR negative (0 points), and HER 2 positive on immunohistochemistry (Fig. 2.).

Fig. 1. Breast tru-cut biopsy high-grade invasive carcinoma, H&E x 100.
The pulmonary X-ray performed on admission revealed 15mm formation in the upper left pulmonary field. The patient was referred for further evaluation to a PET CT examination, where were seen two metabolically active formations: one in the right breast (32/24mm and SUV max 8.7) (Fig. 3.) and one in the left lung (19/16mm and SUVmax 5.1) (Fig. 4.) Differential diagnosis was made between new primary cancer, metastases from breast cancer or benign lesion.

The multidisciplinary tumour board (MTB) first referred the patient to a Thoracic surgery clinic, where an upper left lobectomy was performed. The final histology showed primary adenocarcinoma of the lung (Fig. 5.), EGFR negative, pT1aN0. The patient was again presented at MTB, where a neoadjuvant therapy for breast cancer was recommended. She underwent 3 cycles of Cyclophosphamide and Epirubicin followed by 4 cycles of Docetaxel, Trastuzumab, and Pertuzumab.

After the end of neoadjuvant therapy, the patient was scheduled for surgery in November 2017 - lumpectomy with axillary clearance. The final pathology report showed a full pathologic response, 12 removed lymph nodes without metastases, ypT0N0. She received also postoperative radiotherapy, Trastuzumab (up to 1 year) and aromatase inhibitor (up to 5 years). Currently, the patient is in no evidence of the disease state.
DISCUSSION

Synchronous primary malignancies are hard for diagnosis and worsens the patient’s prognosis. [5] We presented a rare case of early synchronous breast and lung cancer with excellent treatment results.

Breast and lung cancer represent 26.8% and 5.4%, respectively, of the new cancer incidence among women in Bulgaria in 2015. The risk of second cancer following radiotherapy for early breast cancer is well known, especially for second primary lung cancer. [6] Still, their synchronous appearance is very rare and may due to some genetic or environmental factors. There are several case reports in the literature regarding the diagnosis and treatment of synchronous lung and breast cancer.

A study of the multiple primary malignancies involving lung cancer investigates 175 primary lung carcinomas in association with any second primary. Of the accompanying malignancies 64 (36.6%) occurred simultaneously, of which only 3 were in the breast. Synchronous MPM patients demonstrated significantly worse OS than metachronous MPM patients, with median OS rates of 12.9 (range 0.8–86.3) months and 72.8 (range 12.2–391.0), respectively ($P < 0.001$). [5]

Nowadays, pCR rate in HER2 positive cancer is a common event. In 2012 were published the first results of the NeoSphere study: a randomized multicenter, open-label, phase 2 trial comparing 4 different regimens for neoadjuvant treatment of HER2 positive breast cancer. Patients given Pertuzumab and Trastuzumab plus Docetaxel had a significantly improved pCR rate (49 of 107 patients; 45.8%), compared with all other groups. [7] Further analysis of this trial suggest that total pCR could be an early indicator of long-term outcome in early-stage HER2-positive breast cancer [8], but fail to find a significant association of any biomarker with pCR and treatment, except high HER2 membrane protein expression. [9]

In 2017 was published a retrospective study evaluating the pathologic complete response in 57 HER2 positive patients treated with neoadjuvant Doxorubicin and Cyclophosphamide followed by Paclitaxel with Trastuzumab and Pertuzumab. The authors reported total pCR (tpCR, defined as ypT0/is ypN0) in 41/57 (72%) of the cases. [10] The pathological complete response has been proposed as a surrogate endpoint for prediction of long-term clinical benefit, such as disease-free survival, event-free survival (EFS) and overall survival (OS) in breast cancer patients. The triple-negative and HER2 positive, hormone-receptor-negative tumours (with the addition of trastuzumab) has shown the strongest association. [11]

In Bulgaria only about 6% of the lung cancer patients are diagnosed in the 1st stage. This is also the stage of 27% of the breast cancer patients. [4] It is proven that the achievement of pCR is increasing with a higher number of cycles given before surgery and results in significantly higher disease-free and overall survival [12]. In Bulgaria, as we have previously reported, in the vast majority of cases, surgery is performed after 4 cycles of pre-operative systemic therapy [13]. In this situation, pCR is rarely observed.

CONCLUSION
Excellent prognosis still can be achieved also in patients with MPM, when the right management of the patient is applied.

REFERENCES:


