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]
Fig. 2. Invasive BC, HER2 positive staining x 400.

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.

Fig. 3. PET CT visualization of the lesion in the breast.

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.), EGRF 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.

Fig. 4. PET CT visualization of the lesion in the lungs.

Fig. 5. Lung adenocarcinoma, H&E x 100.

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 worsen 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 preoperative 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:

1. Irimie A, Achimas-Cadariu P, Burz C, Puscas E. Multiple primary malignancies—epidemiological analysis at a single tertiary institution. J Gastrointestin Liver Dis. 2010 Mar; 19(1):69-73. [PubMed] [Crossref]

2. Vogt A, Schmid S, Heinimann K, Frick H, Herrmann C, Cerny T, et al. Multiple primary tumours: challenges and approaches, a review. ESMO Open. 2017 May 2;2(2):e000172. [PubMed] [Crossref]

3. Howe HL (ed). A Review of the Definition for Multiple Primary Cancers in the United States. Workshop Proceedings From December 4–6, 2002, in Princeton, New Jersey. Springfield (IL): North American Association of Central Cancer Registries, May 2003. [Internet]

4. Valerianova Z, Atanasov T, Vukov M. (eds.) Cancer Incidence in Bulgaria, 2014 & 2015. Bulgarian National Cancer Registry. Sofia. 2017 vol.25. [Internet]

5. Li F, Zhong WZ, Niu FY, Zhao N, Yang JJ, Yan HH, et al. Multiple primary malignancies involving lung cancer. BMC Cancer. 2015 Oct 14;15:696. [PubMed] [Crossref]

6. Grantzau T, Overgaard J. Risk of second non-breast cancer after radiotherapy for breast cancer: a systematic review and meta-analysis of 762,468 patients. Radiother Oncol. 2015 Jan; 114(1):56-65. [PubMed] [Crossref]

7. Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncol. 2016 Jun;17(6):791-800. [PubMed] [Crossref]

8. Gianni L, Pienkowski T, Im YH, Tseng LM, Liu MC, Lluch A, et al. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. Lancet Oncol. 2012 Jan;13(1):25-32. [PubMed] [Crossref]

9. Bianchini G, Kiermaier A, Bianchi GV, Im YH, Pienkowski T, Liu MC, et al. Biomarker analysis of the NeoSphere study: pertuzumab, trastuzumab, and docetaxel versus trastuzumab plus docetaxel, pertuzumab plus trastuzumab, or pertuzumab plus docetaxel for the neoadjuvant treatment of HER2-positive breast cancer. Breast Cancer Res. 2017 Feb 9;19(1):16.
10. Singh JC, Mantani A, Barrio A, Morrow M, Sugarman S, Jones LW, et al. Pathologic Complete Response with Neoadjuvant Doxorubicin and Cyclophosphamide Followed by Paclitaxel with Trastuzumab and Pertuzumab in Patients with HER2-Positive Early Stage Breast Cancer: A Single Center Experience. Oncologist. 2017 Feb;22(2):139-143. [PubMed] [Crossref]

11. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014 Jul 12;384(9938):164-72. [PubMed] [Crossref]

12. Krishnan Y, Al Awadi S, Sreedharan PS, Sujith Nair S, Thuruthel S. Analysis of neoadjuvant therapies in breast cancer with respect to pathological complete response, disease-free survival and overall survival: 15 years follow-up data from Kuwait. Asia Pac J Clin Oncol. 2018;12(1):e30-7. [PubMed] [Crossref]

13. Vasileva M, Masliankov S, Vlahova A, Genadieva M, Pavlov V, Zahariev Z, et al. [Pathologic response to preoperative systemic therapy in breast cancer patients- achievable prognostic factor.] [in Bulgarian] Book from the 16th National congress of Surgery, Bulgarian Surgical Congress Society. 2018; 1:632-642. [Internet]

Please cite this article as: Vasileva- Slaveva M, Vlahova A, Valev S, Konsoulova A, Masliankov S. Complete response in synchronous early breast and lung cancer. J of IMAB. 2020 Jan-Mar;26(1):2883-2886.
DOI: https://doi.org/10.5272/jimab.2020261.2883

Address for correspondence:
Mariela Vasileva-Slaveva,
Alexandrovska University Hospital, Department of surgery, Medical Faculty, Medical University Sofia,
1, St. Georgi Sofiiski blvd., 1431 Sofia, Bulgaria
E-mail: sscvasileva@gmail.com