



## DUAL PRIMARY MALIGNANCY: A RARE ORGAN COMBINATION

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**ABSTRACT** A 54-year-old female smoker was evaluated for lump over the right breast, fine needle aspiration cytology of which showed infiltrating ductal carcinoma. Investigations also revealed the presence gall bladder mass lesion. The existence of two malignancies having different histopathologies at anatomically distinct sites suggests the diagnosis of dual primary malignancy involving the breast and the gall bladder which, being a rare combination, prompted us to report the case.

## KEYWORDS :

## INTRODUCTION

First incidence of multiple primary cancers in a single patient was reported more than 100years ago. Since then the occurrence of second malignancy in a patient with a known malignant tumour is not uncommon. This phenomenon has been identified with increasing frequency. Two cancer either detected at the same time (synchronous) or one may follow the other after a period of time (metachronous). Although metachronous tumours are becoming increasingly frequent because of increase in life expectancy, improvement in diagnostic techniques and comprehensive screening protocols in cancer patients yet existing primary involving both organs in a single patient is a rarity in medical literature, prompting us to publish this case.

## CASE REPORT

A 54-year-old female patient was admitted IN johal multispeciality hospital for evaluation of a lump over the right breast since 6 months which was painless and had gradually increased in size over the last 3 months. She also had anorexia but no significant weight loss. She . There was no history of cigarette or alcohol intake. She did not have any family history of breast or ovarian cancer. She had been postmenopausal since the last 2 years and did not give history of oral contraceptive pill (OCP) use. On examination, a mass measuring approximately 4cm\*4cm was seen over the right upper quadrant of the breast (Figure 1). The mass was hard in consistency, nontender, and freely mobile over the chest wall withfixity to the skin above. The skin overlying the lump was normal . There was no nipple or areolar discharge. There were palpable anterior axillary lymph nodes with no supraclavicular lymphnode . CBC,LFT,RFT,chest x ray were normal limit. . A contrast- enhanced computed tomography of abdomen (CECT) revealed a soft tissue mass in gallbladder. Fine needle aspiration was done from the breast lump which was suggestive of infiltrating ductal carcinoma breast. MRM WAS DONE ALONGWITH RADICAL CHOLECYSTECTOMY ON 1/11/2021. HPE of breast specimen showed infiltrating ductal carcinoma breast . Lymph nodes show chronic lymphadenitis. HPE of gall bladder showed adenocarcinoma A diagnosis of a synchronous dual primary cancer of gall bladder and breast was made. The patient was advised hormonal manipulation based on ER, PR, HER- 2 markers for her breast cancer which she refused. She was on regular follow up for 3 months and clinically there was no evidence of disease but then she didnt turned uo for follow up.

## DISCUSSION

Multiple primary malignancies in a single patient were first described in 1879 by Billroth [1]. The neoplasms may be limited to a single organ or, involve multiple and anatomically separate organs. The North American Association of Central Cancer Registries (NAACCR) classifies multiple primary tumors into two categories: (1) *Synchronous*, in which the cancers occur at the same time (the Surveillance Epidemiology and End Results Program (SEER) definition is within two months) and (2) *Metachronous*, in which the cancers follow in sequence, that is, more than two months apart [2]. Metachronous primary malignancies are becoming increasingly

common because of an increase in the number of elderly cancer survivors, greater awareness, and improved diagnostic modalities. In comparison, synchronous tumors occur uncommonly, with the most common site for synchronously existing multiple tumors being the breast.

Whether the second lesion is truly a primary or represents metastases is difficult to decide and for this the Warren and Gates criteria (1932) are used which proposed that a diagnosis of multiple primary malignancies requires the following [1]:(1)each tumor should present a definite picture of malignancy;(2)each tumor should be histologically distinct;(3)the possibility that one is a metastasis of the other must be excluded.

The pathophysiology behind the occurrence of multiple primary malignancies has been theorized to be common-carcinogen induced multiple cancers in an exposed epithelial surface, called "field-cancerization" as seen in head-neck tumors, as a late side effect of treatment used to treat the first tumor, and a genetic predisposition to neoplasia [6]. Other possible causal factors include persistent carcinogen exposure from environment, progressive ozone depletion and effects of ionizing radiation, increased use of organ transplant, and the increasing use of newer treatment modalities like hormonal manipulation, target therapies, genetic manipulation, and immunomodulators [7].he prevalent coincidence of microsatellite instability suggests that the genetic defect of mismatch repair deficiency may be responsible for a small subset of double cancers of the colorectum and stomach. Germ-line mutations of P53, tumor suppressor gene, were found in children and young adults with a second malignant neoplasm.An autopsy series has reported that a greater percentage of multiple primary cancers occur in the same organ or in organs of the same system rather than in unrelated organs [8]. Breast and lung cancers are the two most frequent cancers detected in women, yet a double primary cancer involving the two has been reported only rarely in the literature. Kurishima et al. in their study of 98 lung cancer patients having synchronous and/or metachronous malignancies did not report even a single patient with breast cancer as the second tumor [9].

The occurrence of dual primary malignancies is not rare. With lung cancer, finding a tobacco related cancer like cancer of larynx and bladder is possible. In this patient, the presence of small cell lung cancer may be explained by smoking and exposure to domestic biofuels, but these do not account for breast cancer, a nontobacco associated neoplasm. This rare coexistence of lung with breast cancer may therefore be due to coincidence, which prompted us to report this case.

In conclusion, this case highlights the fact that the presence of a lesion anatomically away from the primary malignancy should be labelled as a metastasis only after detailed evaluation; otherwise, there is a possibility of missing a synchronous primary malignancy. treatment strategies in case of synchronous double malignancy depend on

treating the malignancy that is more advanced first or sometimes both could be treated simultaneously. In our case, we concluded that a synchronous double malignancy can be treated successfully. Both sites should be treated fully as if they were occurring separately considering toxicities.

## REFERENCES

1. S. Warren and D. Gates, "Multiple primary malignant tumor: a survey of the literature and a statistical study," *American Journal of Cancer*, vol. 51, pp. 1358–1414, 1932.
2. "A Review of the Definition for Multiple Primary Cancers in the United States," in *Workshop Proceedings From December 4-6, 2002 in Princeton, New Jersey*, H. L. Howe, Ed., North American Association of Central Cancer Registries, Springfield, Ill, USA, 2003.
3. M. J. Hayat, N. Howlader, M. E. Reichman, and B. K. Edwards, "Cancer statistics, trends, and multiple primary cancer analyses from the surveillance, epidemiology, and end results (SEER) program," *The Oncologist*, vol. 12, no. 1, pp. 20–37, 2007.
4. M. P. Sang, K. L. Min, W. J. Kyu et al., "Prediagnosis smoking, obesity, insulin resistance, and second primary cancer risk in male cancer survivors: National Health Insurance Corporation Study," *Journal of Clinical Oncology*, vol. 25, no. 30, pp. 4835–4843, 2007.
5. Y.-Y. Liu, Y.-M. Chen, S.-H. Yen, C.-M. Tsai, and R.-P. Perng, "Multiple primary malignancies involving lung cancer—clinical characteristics and prognosis," *Lung Cancer*, vol. 35, no. 2, pp. 189–194, 2002.
6. W.-C. Hsieh, Y.-M. Chen, and R.-P. Perng, "Temporal relationship between cancers of the lung and upper aerodigestive tract," *Japanese Journal of Clinical Oncology*, vol. 27, no. 2, pp. 63–66, 1997.
7. I. Mehdi, A. H. Shah, M. S. Moona et al., "Synchronous and metachronous malignant tumours expect the un-expected," *Journal of the Pakistan Medical Association*, vol. 60, no. 11, pp. 905–909, 2010.
8. S. Watanabe, T. Kodama, Y. Shimosato et al., "Multiple primary cancers in 5,456 autopsy cases in the National Cancer Center of Japan," *Journal of the National Cancer Institute*, vol. 72, no. 5, pp. 1021–1027, 1984.
9. K. Kurishima, H. Satoh, S. Homma et al., "Multiple primary malignancies in patients with lung cancer," *Radiology and Oncology*, vol. 39, no. 1, pp. 49–53, 2005.
10. S.-P. Luh, C. Kuo, and T. C.-Y. Tsao, "Breast metastasis from small cell lung carcinoma," *Journal of Zhejiang University: Science B*, vol. 9, no. 1, pp. 39–43, 2008.
11. Y. Chang, W. Johnson, K. Karamlou et al., "The evaluation and treatment implications of isolated pulmonary nodules in patients with a recent history of breast cancer," *The American Journal of Surgery*, vol. 191, no. 5, pp. 641–645, 2006.
12. Howe HL, editor. A review of the definition for multiple primary cancers in the United States. Workshop Proceedings from December 4-6, 2002, in Princeton. North American Association of Central Cancer Registries: New Jersey, Springfield (IL); May 2003.
13. Kimura K, Shinmura K, Hasegawa T, Beppu Y, Yokoyama R, Yokota J. Germline p53 mutation in a patient with multiple primary cancers. *Jpn J Clin Oncol* 2001;31:349-51.
14. Bongers V, Braakhuys BJ, Tobi H, Lubsen H, Snow GB. The relation between cancer incidence among relatives and the occurrence of multiple primary carcinomas following head and neck cancer. *Cancer Epidemiol Biomarkers Prev* 1996;5:595-8.
15. Mitchell ME, Johnson JA, Wilton PB. Five primary synchronous neoplasms of the gastrointestinal tract. *J Clin Gastroenterol* 1996;23:284-8.
16. Verstovsek S, Verschraegen CF, Edwards CL, Malpica A, Kavanagh JJ, Ross MI, et al. Synchronous primary cancers of the breast and cervix: Planning multidisciplinary primary treatment [clinico-pathological conference]. *Am J Clin Oncol* 2000;23:99-103.
17. Masood I, Bhargava R, Ahmad Z, Sharma DK, Sherwani R, Shirazi N. A Case of double malignancy - Carcinoma Lung and rhabdomyosarcoma - in a 90- year-old male. *J Indian Assoc Commun Med* 2005;6:167-70.
18. Grosjean P, Monnier P. Impact of diagnosis and treatment of early stage secondary tumors on outcome for the oncologic ORL patient. *Schweiz Med Wochenschr* 2000;116:43S-6S.
19. Di Martino E, Sellhaus B, Hausmann R, Minkenber R, Lohmann M, Esthofen MW. Survival in second primary malignancies of patients with head and neck cancer. *J Laryngol Otol* 2002;116:831-8.