Case Report: Gynaecology

Synchronous Primary Malignancies at Two Sites: A Rare Case Presentation

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ABSTRACT

The diagnosis of multiple primary malignancy (MPM) is not uncommon. Nevertheless synchronous MPM involving endometrium and lungs is an extremely unusual event.

We report a case of 54 years old female patient who presented with abnormal uterine bleeding and was diagnosed as a case of fibroid uterus. She was incidentally found to have a nodular mass in left lung in chest x-ray. Contrast Enhanced Magnetic Resonance Imaging (CEMRI) and Whole body 18F-fluro deoxy glucose positron emission tomography- computed tomography (18 F-FDG PET-CT) revealed two distinct lesions- one in endometrium and another in left lung. Immunohistochemistry and biopsy from the endometrium and lung lesion were suggestive of endometrioid carcinoma and adenocarcinoma respectively.

Hence, the existence of two malignancies having different histopathologies at anatomically distinct sites suggests the diagnosis of synchronous dual primary malignancy involving the endometrium and the lung, which being a rare combination, prompted us to report this case.

Hence, the possibility of multiple primary malignancies existence should always be considered during pre-treatment evaluation.

Key words: Adenocarcinoma, carcinoma endometrium, immunohistochemistry, malignancies, primary malignancies, synchronous

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Introduction

The incidence of multiple primary cancers is reported to be 0.734% to 11.7%.[1] Despite its increasing rates, multiple primary malignancies (MPM) remain rare. Multiple primary malignancies in a single patient were first described in 1879 by Billroth.[2]

By definition, synchronous primary malignancies means two cancers detected at the same time or within 6 months whereas metachronous primary malignancies means one that follows the other after six months of diagnosis of first tumor.[3] A synchronously existing primary involving both organs in a single patient is a rarity in medical literature, prompting us to publish this case.

However, with the advent of advanced diagnostic imaging modalities, immunohistochemistry as well as increased efficacy of cancer therapy, the occurrence of multiple primary malignancy (MPM) is being identified with increased frequency[4] and also managed simultaneously and effectively.

Case

A 54 years old female, P2L2 with newly diagnosed Type II DM presented to outpatient department with complaint of abnormal uterine bleeding since past 2 years. There was no history of smoking. She did not have any family history of breast, endometrial or ovarian cancer. Her general and systemic examinations were normal. On per speculum examination cervix looked healthy while on per vaginal examination uterus was bulky and fornices were free. Basic blood investigations were normal.

On ultrasonography of pelvis uterus was bulky (10 x 5.9 x 4.9 cm) with three small fibroids; largest measuring 2.2 x 2.4 cm and 2.2 x 1.9 cm with endometrial thickness of 8.6 cm. Hence, hysteroscopy followed by dilatation and curettage was planned.

While evaluating the patient for surgical fitness chest X-ray revealed an incidental finding of a nodular lesion in left lower zone. Hence, a High Resolution Computed Tomography (HRCT) was performed showing a 3.2 x 2.4 cm nodular lesion with spiculated margins at lateral basal segments of left lower lobe (Figure 1). Endobronchial Ultrasound guided Trans Bronchial Needle Aspiration (EBUS- TBNA) revealed no evidence of cancer, tuberculosis and gram stain cultures. The patient underwent a Contrast Enhanced Magnetic Resonance Imaging (CEMRI) which revealed similar findings in left lung and uterus. Also, there was an asymmetric thickening of endometrium towards the left side likely due to endometrial polyp.

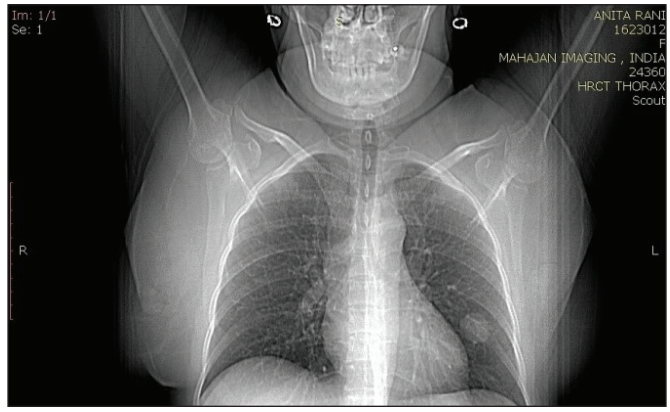

Figure 1: showing soft tissue attenuation nodular lesion; measuring 3.2 x 2.4 cm with lobulated outline and spiculated margins in lateral basal segment of left lower lobe, peripherally in subpleural location.

Further evaluation with Fluorodeoxyglucose whole body Positron Emission Tomography Computed Tomography (FDG PET-CT) scan conveyed FDG avid pleural based nodular lesion in lateral basal segment of lower lobe of left lung (Figure 2) and FDG avid hypodensity within the endometrial cavity (Figure 3).

Histopathology of CT guided lung biopsy indicated Non small cell carcinoma of lung; possibly adenocarcinoma. This was further supported by immunohistochemistry in which Thyroid Transcription Factor-1 (TTF-1), Sytokeratin 7 (CK-7) were strongly positive and Cytokeratin-20 (CK-20), Estrogen Receptor (ER), Progesterone Receptor (PR), Paired-Box Gene 8 (PAX-8) were negative indicating non small cell carcinoma of lung- adenocarcinoma.

After 5 days patient underwent hysteroscopy with dilatation and curettage. Histopathology of endometrial biopsy revealed endometrial carcinoma. Whereas, Estrogen Receptor (ER)- positive >90% moderate intensity, Progesterone Receptor (PR)- positive >90% high intensity, p53- focal patchy positive (wild type), p16- focal patchy positive, Napsin- negative in immunohistochemistry was suggestive of Endometroid carcinoma (FIGO grade I). The diagnosis of synchronous dual malignancy involving lungs and endometrium was thus conferred.

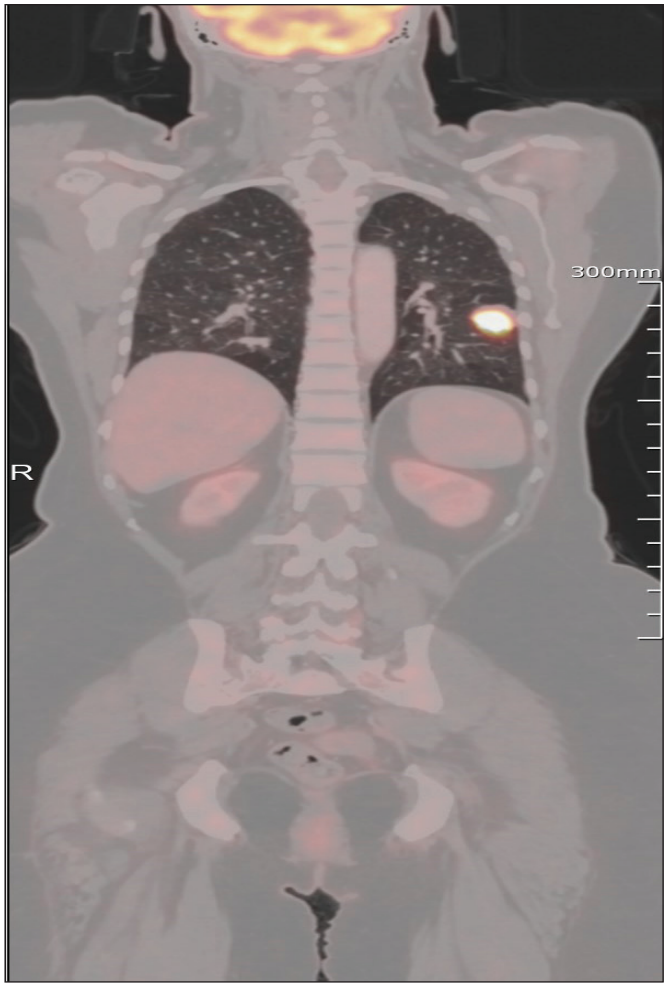

Figure 2: Showing pleural based nodular soft tissue lesion with spiculated margins noted in the lateral basal segment of lower lobe of left lung measuring 3.3 x 2.4 x 2.1 cm in size in PET-CT scan. The lesion is tethered to the left oblique fissure with fibrotic strands.

Patient underwent Video Assisted Thoracoscopic Surgery (VATS)- left lower lobectomy, mediastinal dissection along with Staging laparotomy for carcinoma endometrium- Hysterectomy with bilateral salpingoophorectomy and bilateral pelvic lymph node dissection with peritoneal washings in the same sitting. Intraoperative and postoperative period was uneventful. Histopathology of uterus concluded endometroid carcinoma of endometrium (Figure 4) involving fundus and body while regional lymph nodes were free of tumor (Stage I; Grade 1). Whereas, histology of left lower lobe revealed invasive solid adenocarcinoma (Figure 5); with no involvement of lymph nodes. (Stage I; Grade 2).This confirms that the patient had two synchronous primary cancers.

Initially we thought that we were dealing with carcinoma endometrium with metastasis to lungs or

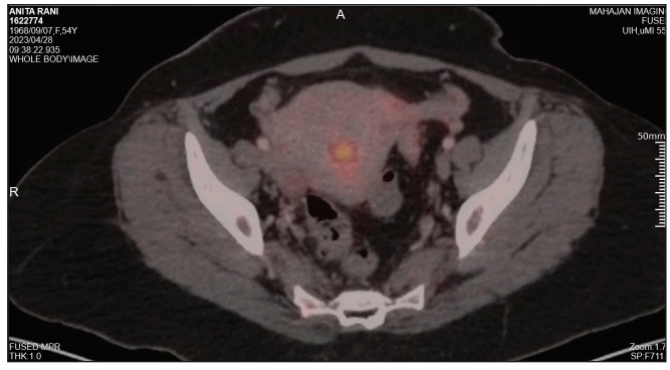

Figure 3: FDG avid hypodensity noted within the endometrial cavity

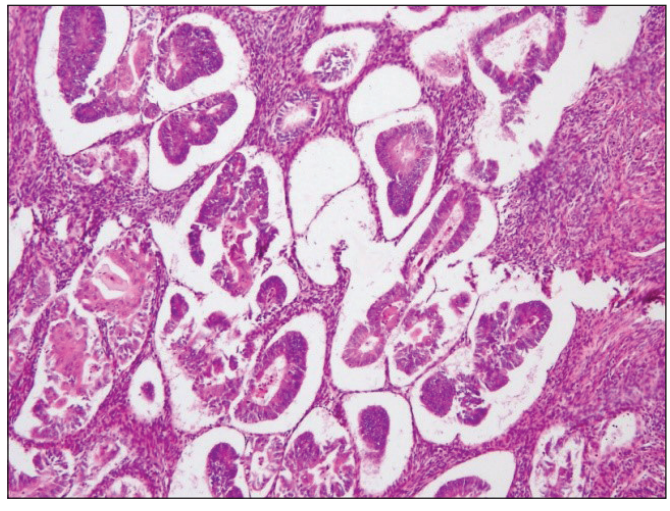

Figure 4: shows endometrial glands lying back to back with intervening stroma; suggestive of endometrial carcinoma

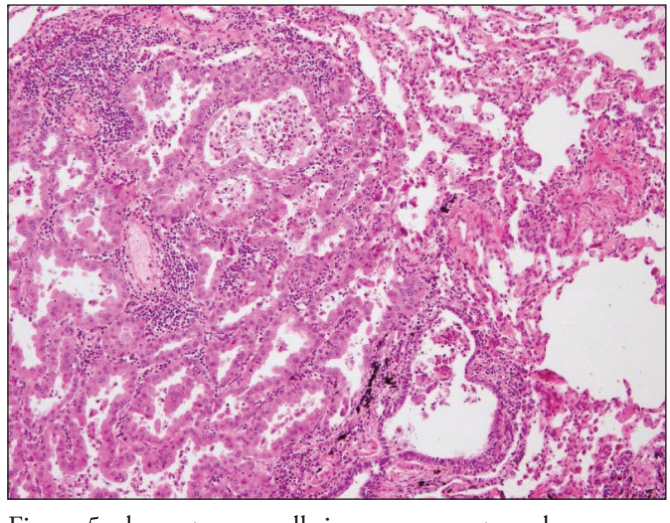

Figure 5: shows tumor cells in groups, nests and some forming glandular pattern. These cells are round to oval with high N/C ratio, hyperchromatic nuclei, moderate cytoplasm and prominent nucleoli in some. There is intense infiltration by inflammatory infiltrate; suggestive of adenocarcinoma of lung.

vice-versa which could have changed our diagnosis and staging but the histology and Immunohistochemistry (IHC) of both the tumors pointed out that we are dealing with two primary cancers. Henceforth, this gave us confidence to operate on both the primary tumors at the same sitting. Our patient stood the procedure well. Her postoperative period was uneventful and was discharged in fair condition.

Till date she is doing fine and is receiving chemotherapy with Pemetrexed and Carboplatin for 4 cycles followed by Osemertinib for lung carcinoma. Meanwhile, in view of Stage I, Grade I endometroid carcinoma she will be followed up every 3 monthly for first two years, then every 6 months for three years, thereafter annually.

Discussion

Metachronous primary malignancies are becoming increasingly common because of an increase in the number of elderly populations, 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.[5] If initial primary is the breast, the percentage of patients expected to develop multiple primaries is 10% and for the lung it is 4%.[6] Liu et al. reported that the most common tumors accompanying lung cancer were in the aerodigestive tract (in descending order of frequency): larynx, nasopharynx, esophagus, oral cavity, hypopharynx, followed by colorectal and cervical malignancies.[7]

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 following2: (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. Though the mechanism involved in the development of multiple primary cancer has not been clarified, some factors such as heredity, constitution, environmental and immunological factors, carcinogenic, viruses, radiological and chemical treatments have been implicated.[8,9]

The outcome of management of patients with dual malignancies should be determined independently based upon the stage of each cancer.[10] The choice of treatment should depend upon the tumor location, involved curative surgical resection of each cancer, radiotherapy and chemotherapy. If surgery is required for both the tumors, it can be done so simultaneously in a majority of cases with low rate of morbidity and mortality as done in our case.[11]

Differential diagnosis for the patient in our case included lung metastases from the endometrium primary or vice versa. Lung metastases from endometrial neoplasms are very common, accounting for about 20-25% of all endometrial malignancies.[12,13] Double primary cancer is a more reasonable diagnosis in this case since the histopathology and immunohistochemistry of the endometrium was an endometroid carcinoma and that of the lung mass was adenocarcinoma thus ruling out any possibility of metastasis from one site to the other. This assumption is also in agreement with the North American Association of Central Cancer Registries (NAACCR) definition that "multiple lesions of different histologic types occurring in different sites are considered as separate primaries whether occurring simultaneously or at different times".[14]

Conclusion

Multiple primary malignancies seem to be diagnosed in a higher incidence than that predicted due to the increase in life expectancy of general population—a boon of advancements in cancer therapeutics— and to the more comprehensive screening protocols used in cancer patients. The study of this case can provide useful information regarding the development of effective screening and surveillance protocols, with the goal to treat patients effectively.

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 and possible effective management of the patient.

In our case, patient was planned for hysteroscopy followed by dilatation and currettage but as a part of her pre-operative workup her chest x-ray revealed an incidental finding of nodular lesion in left lungs. Hence, this case highlights a thorough pre-operative work

up of any patient undergoing surgery. Microscopic findings and immunohistochemistry proved us that we were dealing with two primary cancers and further helped us in its effective management. Both the primary cancers were in Stage I early grade. Thus, operating the patient simultaneously saved the patient from having any adjuvant therapy.

This case also highlights that proper workup of a patient is essential in managing the disease. Otherwise, we would have labelled her a case of Stage IV carcinoma endometrium and managed her accordingly. But, careful preoperative workup and immunohistochemistry helped in diagnosing this case as a synchronous primary malignancies. As a result we could provide appropriate and timely surgical management to the patient.