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A RARE SYNCHRONOUS PRESENTATION OF DOUBLE PRIMARY MALIGNANCY

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ABSTRACT

Background: Patients which have diagnosed with a cancer, have a life time risk for developing another de novo malignancy depending on various inherited, environmental and iatrogenic risk factors. Cancer victims could survive longer due to settling treatment modalities, and then would likely develop a new metachronous malignancy. This article aims to report management of an old age female patient affected by dual primary synchronous tumors of the breast and kidney. This combination, to the best of our knowledge, has never been previously reported in the literature, and it raised a series of diagnostic, etiological and therapeutic issues persuading us to carry out a critical review of the literature. Synchronous (SC) diagnosis of double primaries is not very rare in this era of advanced technology where underlying malignancies can easily be detected by the modern imaging techniques. However, the treatment of such patients is quite challenging and often a therapeutic dilemma{1} **Methods:** A hospital based case study done at New Civil Hospital Surat on the patient aged 65 years female, housewife with no co-morbidities like diabetes and hypertension. Came in General Surgery OPD for left breast lump. Multiple imaging and radiological and histological investigations were done revealing double primary malignancy. Multidisciplinary approach for the treatment was planned and executed, involving surgical excision followed by chemotherapy. **Conclusion:** The incidence of multiple primary malignancies has not been rare at all. Screening procedures have especially been useful for the early detection of associated tumors, whereas careful monitoring of patients has treated for primary cancer, and then a good communication between patients and medical care team would certify not only an early detection for secondary tumors, but only finally & subsequently, an appropriate management.{1}

INTRODUCTION

In this report, we describe management of a post menopausal female patient affected by dual primary synchronous tumors of the breast and kidney. This combination, to the best of our knowledge, has never been previously reported in the literature, and it raised a series of diagnostic, etiological and therapeutic issues persuading us to carry out a critical review of the literature.

Case Presentation

A 65 y old post menopausal Asian female belonging to Gujarat presented to Out patient Department , General Surgery Department ,New Civil Hospital Majuragate Surat , with lump over left Breast upper and outer quadrant associated with left axillary mass for 2 years. Patient was admitted, on history taking ,Patient had menarche at around 14 years ,had 6 six births , no abortion , had menopause at 50 years . She had no comorbidities and addiction, no significant family or personal history either. Past medical history was unremarkable. It started as small mass over left breast which gradually grew in past 3-4 months , no discharge , no other associated swelling .

On local examination there was 3x3 sq cm mass was found over left outer and upper quadrant ,non tender, firm consistency , smooth surface , irregular margin , non adherent to skin and adherent to underlying structure , non fluctuant with palpable 4x3sqcm axillary lump over lateral aspect of chest. On Ultrasonography showed:- Nodular marginated solid lesion in left axillary tail region extending upto upper outer quadrant of left breast.p/O Breast mass lymphnodes with loss of normal fatty hilum seen in left axillary region, P/O Breast malignancy with metastasic lymphnodes. Followed by FNAC cytology study positive for DUCTAL CARCINOMA. For further evaluation TRUCUT biopsy was taken of the breast mass histological features are suggestive of Invasive Breast Carcinoma ,IHC negative for PR & Her-2/neu Receptors.

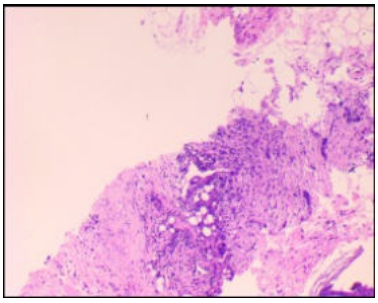

Figure 1 Immunohistochemical image of left breast mass biopsy

Patient then undergone CECT THORAX ABDOMEN PELVIS for evaluation of metastasis suggestive of malignant neoplastic etiology of left breast with Satellite lesion and metastatic lymphadenopathy in right axilla. On delayed scan- Large well defined exophytic hypodense lesion which shows peripheral hyperenhancement in arterial phase with central non-enhancing scar seen in lower pole of right kidney, P/o: Neoplastic mass of RIGHT KIDNEY. The renal mass was further biopsied , on HISTOLOGY AND IHC- There are Tumour cells,

are immunoreactive for CK & CD 68 suggestive of Renal Cell Carcinoma - Probably Clear Cell Variant.

Figure 2 Excised renal mass

Multidisciplinary approach was considered including specialist consultations including team of surgeons , dedicated Pulmonologist and oncologist . First we performed left breast modified radical mastectomy, the specimen sent for HPE confirming the diagnosis of INVASIVE DUCTAL CARCINOMA (pT2N2a) with skin and surrounding structures along with lymphnodes free from tumor cells Followed by Neoadjuvant chemotherapy(NACT) DOXORUBICIN & CYCLOPHOSPHAMIDE FOLLOWED BY PACILITAXEL 4 cycles each Then patient kept for left sided partial nephrectomy{figure 2} with Histopathological confirming the diagnosis of CLEAR CELL RENAL CELL CARCINOMA with International society of Urological Pathology GRADE 1, PATHOLOGICAL GRADE pT1a Followed by NACT mentioned above at present

DISCUSSIONS

The ICMR-NCDIR-NCRP pulls the data through 36 PBCRs (Population-based cancer registry) and 236 HBCRs (Hospital-based cancer registry). The approximate projected cases of cancer in India were 1,392,179 (~1.4 million) in the year 2020, leading to 850,000 (~0.85 million) deaths due to cancers. The five leading cancers in India, as per reported data, were breast, lung, mouth, cervix uteri, and tongue.[2]

Breast cancer accounts for 12.5% of all new annual cancer cases worldwide, making it the most common cancer in the world.[3]From being fourth in the list of most common cancers in India during the 1990s, it has now become the first.[4] Initial criteria of Multiple primary Malignant neoplasm MPMN was formulated by Bilroth in 1889 , at present Warren and Gate criteria is used for the diagnosis of Multiple primary Malignant neoplasm MPMN Multiple tumors with different pathogenetic origin is termed as Mulitiple primary malignant neoplasms (MPMNs), or multiple primary cancers. In 19th century the phenomenon of MPMN was first described by Billroth {5} and since then several cases of double or even triple primary malignant neoplasms have been reported. Neoplasms can be synchronous or metachronous can appear in a single organ or can be in multiple organs concurrently. Moertel (6) defined synchronous neoplasms as those that occur within 6 months from the diagnosis of a previous malignant tumor while metachronous neoplasms as neoplasms that appear 6 months after the first diagnosed tumor (6). Multiple changes in the definition have been proposed, the diagnosis of MPMNs that is widely accepted is based on the criteria described by Warren and Gates (3).

Warren and Gates Criteria for Diagnosis of Double Primary Malignancies.

1. Histological confirmation of malignancy in both the index and secondary tumors.
2. There should be at least 2 cm of normal mucosa between the tumors. If the tumors are in the same location, then they should be separated in time by at least five years.
3. Probability of one being the metastasis of the other must be excluded.

Nowadays, multiple primary cancers are not rare entities. Improved cancer care and increased survival have led to an increase in the number of patients developing multiple cancers.

While it is possible to eliminate risk factors such as smoking, alcohol consumption and unhealthy lifestyle, not-modifiable risk factors such as the genetic susceptibility, the state of immune deficiencies and the sometimes-irreversible effects of anticancer therapies cannot be managed.

Although no familial history or carcinogenetic factor could be evidenced, the occurrence of multiple tumors, especially the synchronous ones, is unlikely to be fortuitous.

Patients who develop multiple cancers may not fall into one of the hereditary syndromes, but it is possible that there are unknown and/or rare genetic predispositions that determine the development of multiple tumors. For this reason, all multiple cancer patients should be followed-up for the development of subsequent cancers.

A complete pre-operative evaluation and interdisciplinary collaboration can always guarantee the best possible treatment for a patient.

Nowadays, the description of case reports is of fundamental importance since they strongly contribute to the progress of medical knowledge, generating new hypotheses and acting as stimulus for the scientific community to verify them. This study portrays a particularly rare clinical picture and provides first evidence of efficacy of a therapeutic protocol that deserves to be investigated in more detail.

In Table 2, a few examples of patients with SC multiple primaries are summarized to illustrate the difficulties that arise in the daily clinical practice.[10]

Patient characteristics	Malignancy 1	Malignancy 2	Therapeutic dilemma	Current management strategy
60-year-old male, former smoker	SCLC Progression After 6 cycles of cisplatin/etoposide	Aplastic anemia Diagnosed 4 months after completion of cisplatin/ etoposide	Chemotherapy at progression of SCLC not possible due to grade 4 neutropenia and thrombocytopenia in the setting of aplastic anaemia Immunosuppressive therapy for aplastic anemia with possible negative impact on SCLC	Supportive treatment with eltrombopag for thrombocytopenia In case of stabilisation of pancytopenia, evaluation of second line therapy for SCLC
71-year-old man, hereditary hemochromatosis	CRPC with bone and lymph node metastases	RCC with lung metastases	Drugs active in for CRPC different than agents in RCC TKI used for RCC endocrine drugs (abiraterone/ enzalutamide) used for CRPC Combinations not tested, no safety data, possible drug–drug interactions, expensive combinations	Alternating treatment for the two malignancies, for example, TKI for 3–4 months for mRCC, then interruption and treatment for mCRPC for 3–4 months depending on the most significant tumour
64-year-old man, former smoker	NSCLC stage IIIB	Rectal cancer stage I	Chemotherapy regimens active in NSCLC generally not active in rectal cancer NSCLC stage IIIB prognosis-defining, but untreated rectal cancer bears high risk of local complications (e.g., bowel obstruction)	Curative resection of rectal cancer (node-negative) with protective colostomy Chemoradiation with curative intent for NSCLC (IIIB)
65-year-old woman, former smoker	NSCLC, metastatic to lymph nodes and bone, KRAS proto-oncogene (KRAS)-mutated, PD-L1 expression 0%	AML Diagnosed simultaneously with NSCLC	Chemotherapy for NSCLC not possible due to grade 4 neutropenia in the setting of AML State-of-the art treatment for AML in the setting of metastatic NSCLC	Treatment with azacitidin for AML In case of stabilisation of AML, evaluation of treatment for NSCLC (checkpoint inhibitor rather than chemotherapy due to limited bone marrow reserve)

SCLC=Small cell lung cancer, NSCLC=Non-small cell lung cancer, AML=Acute myeloid leukaemia, KRAS=Kirsten rat sarcoma viral oncogene homolog, PD-L1=Programmed death receptor ligand-1, CRPC=Castration-resistant prostate cancer, RCC=Renal cell carcinoma, TKI=Tyrosine kinase inhibitor, mRCC=Metastatic RCC, mCRPC=Metastatic CRPC

CONCLUSION

In conclusion, second primary malignancy is not uncommon. With advanced diagnostic and staging modalities and progress in the management of common cancer, the detection rate of second primary malignancy has increased. with multidisciplinary approach extension in expected life years is possible.

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