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Multiple Primary Malignancies: Metastatic Renal with Early Breast and Endometrial Cancers: A Case Report

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Abstract

Double primary malignancies could be divided into two categories, depending on the interval between tumor diagnoses. A secondary malignancy could be defined as a new cancer that has occurred as a result of previous treatment with radiation or chemotherapy. Second primary malignancy can occur at any age but it's commonly at old age. A 46 premenopausal female patient presented to our outpatient clinic complaining from a mass in her right breast, routine metastatic work-up for distant metastasis declared multiple hepatic metastases, RT renal mass, and bone metastases. Palliative radiotherapy to tender and weight bearing sites followed by 4 cycles of systemic chemotherapy FEC regimen were received. Tru-cut needle biopsy from renal mass detected renal cell carcinoma of clear cell type, the patient started sunitinib and tamoxifen with bisphosphonate (Zoledronic acid), assessment of the response revealed reduction of the size and number of HFLs, and the size of renal mass, so the patient was decided to do cytoreductive nephrectomy and then continued on TAM and sunitinib. Collectively, due to the rising incidence of multiple primary malignancies, further studies should be done not only for better clinical evaluation and treatments but also for accurate determination of possible causes, pathogenesis, effective managements and screening programs.

Keywords

Renal Cell Carcinoma, Breast Cancer, PET/CT, Double Malignancies

1. Introduction

In general, the incidence of double primary malignancy is not considered rare [1] [2]; the risk of second cancer has been 10% at 20 years and 26% at 30 years

following Hodgkin disease treatment [3], and 3.8%. At 10 years versus 7% at 15 years for patients treated with doxorubicin-based regimens for breast cancer [4]. Meta-analyses demonstrated a frequency of second primary malignancy of 3% - 5%, third malignancy as 0.5%, and fourth malignancy, namely, quadrant tumor (QT), as 0.3%, in different organ with different histogenesis [5].

Double primary malignancies could be divided into two categories, depending on the interval between tumor diagnoses [6]. Synchronous malignancies were second tumors which have been occurring either simultaneously, or within 6 months after the first malignancy while metachronous malignancies were secondary tumors that have developed after 6 months, or even more than that from the first malignancy.

Warren and Gates [7] [8] [9] [10] defined the criteria for diagnosis of double primary malignancies based on histologic confirmation of primary and secondary tumors, there should be at least 2 cm of normal mucosa and separated by at least 5 years in time if both tumors in the same location, and the probability of second tumor being metastasis of the primary one must be excluded.

A secondary malignancy could be defined as a new cancer that has occurred as a result of previous treatment with radiation or chemotherapy. Depending on the schedule of treatment, the most common secondary cancers were skin cancer, breast cancer, acute leukemia, colorectal, lung and stomach cancer. Second primary malignancy can occur at any age but it's commonly at old age [11].

We aimed from this case report to set forth a rare case of triple malignancy, and to what extent our treatment was successful especially the combination of tamoxifen and sunitinib.

2. Case Report

A 46 premenopausal female patient presented to our outpatient clinic complaining from a mass in her right breast. On physical examination; a mass about 3 cm in diameter in the upper outer quadrant with palpable axillary lymph nodes, palpable right renal mass with tenderness at right shoulder, lumbo-sacral spine, tru-cut needle biopsy revealed infiltrating duct carcinoma, NOS, grade I (**Figure 1**), routine metastatic work-up for distant metastasis including TC-99m whole body bone scan, MSCT chest and pelviabdomin with contrast that declared multiple hepatic metastases with restricted diffusion in segments VIII, VII, VI, and IV varying in size from 1 - 3 cm, **Figure 2** and **Figure 3**, with RT renal mass about 6 cm in diameter, **Figure 2** and **Figure 3**, and randomly distributed foci of tracer uptake intensities keeping with bone metastases involving right shoulder, sternum, upper dorsal, both right and left hips, iliac bones, right femoral shaft, and a big doughnut destructive lytic lesion with soft tissue component at sacral region **Figure 3**. The patient was decided to be metastatic breast cancer when Immunohistochemistry were done and revealed luminal A breast cancer, hence the patient after taking her consent for treatment; started urgent palliative radiotherapy to tender and weight bearing sites followed by 4 cycles of

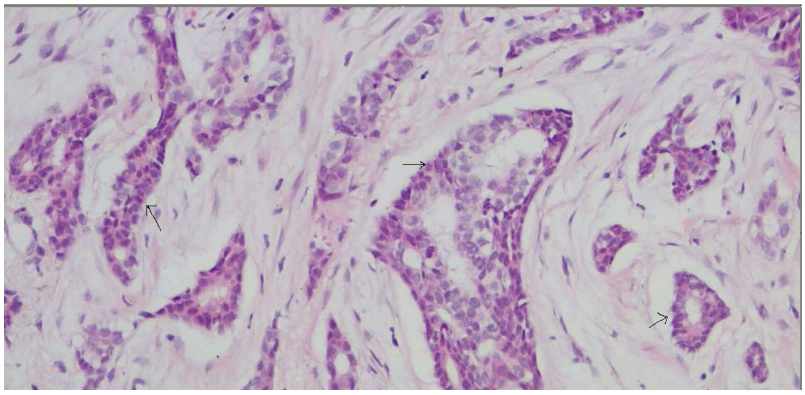

Figure 1. Infiltrating duct carcinoma, NOS, grade 1, ×20, H & E. stain.

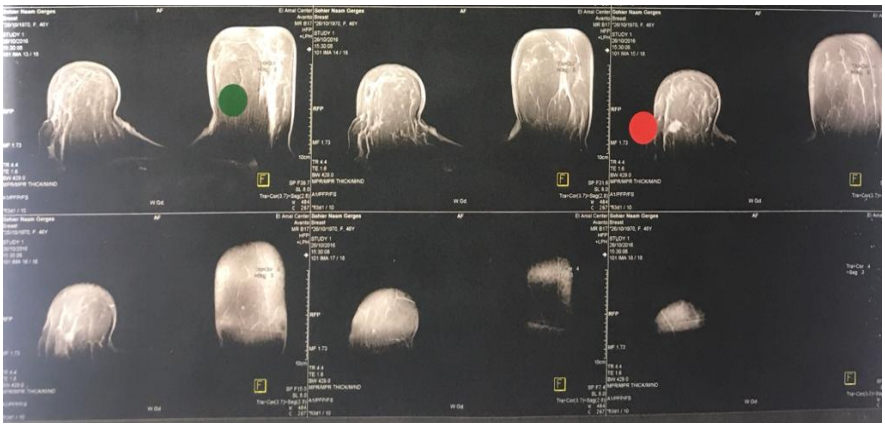

Figure 2. MRI breast showing breast mass the pathology reveal infiltrating duct carcinoma.

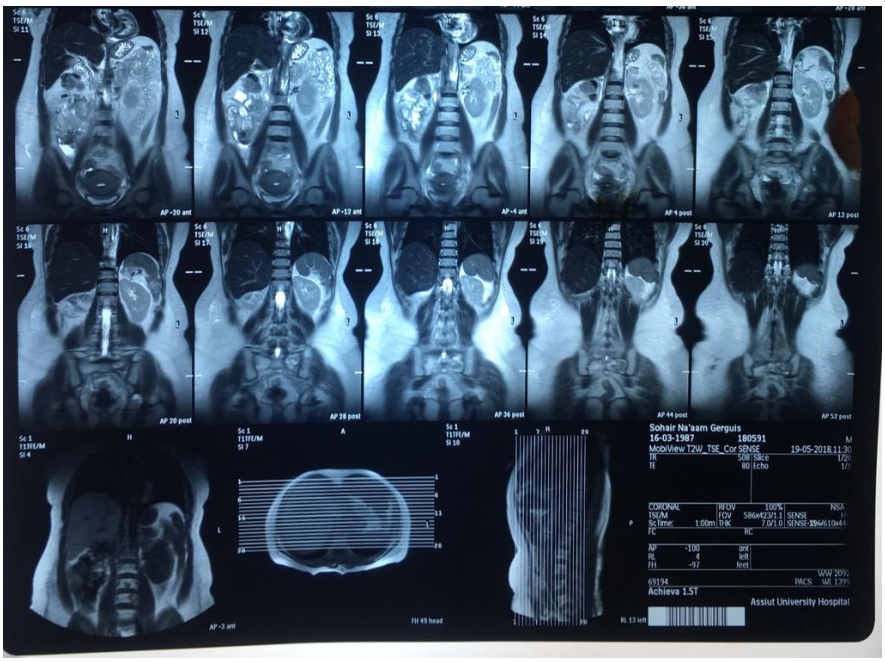

Figure 3. Whole body MRI showing renal mass at lower pole with pathology of clear RCC with hepatic and bony metastasis.

systemic chemotherapy FEC regimen, assessment demonstrated complete disappearance of breast and axillary lesions, improvement of bone pain, but with persistence of renal and hepatic lesions, tru-cut needle biopsy from renal mass detected renal cell carcinoma of clear cell type and Immunohistochemistry proved positive vimentin and negative cytokeratin, systemic CTR was stopped and the case was considered as having double malignancies and of intermediate-risk group based on IMDC criteria of renal risk grouping, the patient started sunitinib and tamoxifen with bisphosphonate (Zoledronic acid), assessment of the response revealed reduction of the size and number of HFLs, and size of renal mass, so the patient was decided to do cytoreductive nephrectomy and then continued on TAM and sunitinib with performance status of 1 - 2, toxicities varied from grade 2 - 3 neutropenia, 1 - 2 fatigue, mild to moderate neuropathy, with stabilization of the response, after one year of postoperative treatment, patient developed vaginal bleeding with severe back pain where dilatation and curettage of endometrium were done with histopathology of atypical endometrial hyperplasia but bleeding was not controlled except after total abdominal hysterectomy and bilateral salpigo-opherectomy, PET/CT was done later on revealed only single HFL with SUV of 10 and size of 1.2 cm and mild activity 5 - 6 of right shoulder and sternal lesion, **Figure 4** and **Figure 5**, the patient was decided to continue on sunitinib and shift from TAM to aromatase inhibitor (Femara 2.5 mg tablet once daily), at last, the patient started treatment 9/2016 and she is still under follow up treating with aromatase inhibitor and Sunitinib with ECOG PS of 1.

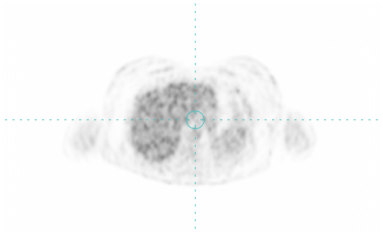

Figure 4. Axial PET image of the liver with low SUV of solitary hepatic focal lesion.

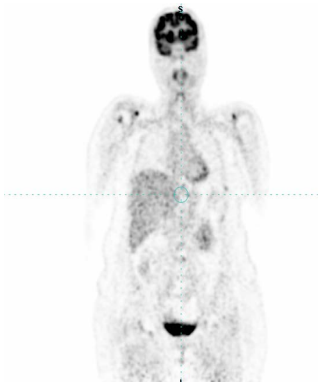

Figure 5. Coronal PET image of the body showing limited SUV activity of rt shoulder lesion.

3. Discussion

Not only environmental factors are responsible for the etiology of double malignancy but also genetic factors, previous chemotherapy, previous radiotherapy, hormonal treatments and others, these factors interacted together to result in these complicated lesions.

Synchronous breast cancer and renal cell carcinoma is very rare and only few reported cases worldwide [12]. Eight cases of synchronous breast primaries with RCC was reported in a population based study done by Jiao F. *et al.* [12], metachronous tumors of breast with renal primary have been reported in literature with both metastatic as well second primaries [13].

Only 3% of metastatic RCC cases reported to have breast metastasis [14], although both breast IDC and RCC were discovered synchronously but we considered our case as having metachronous tumors with early RCC that became metastatic and lastly developed breast cancer, in order to confirm both diagnoses; immunohistochemistry with vimentin and cytokeratin on paraffin breast block were done and was detected to be positive cytokeratin and negative vimentin, furthermore, immunohistochemistry to detect ER and PR on paraffin RCC block were done and detected to be negative.

Based on complete response to chemotherapy and hormonal treatment of breast cancer that was confirmed by PET/CT and the expected short survival from m RCC, we decided not to proceed to mastectomy. Although there is a controversy about the role of CN in m RCC patients receiving targeted therapy [15] as it doesn't change the clinical outcome, but our patient had an intermediate risk at presentation and received a 6-months period of pre-surgical targeted therapy that changed her risk into favorable one and subsequently was decided to do CN.

Now, our patient achieved good clinical response with only solitary hepatic, and few asymptomatic bone metastases, good organ functions, and better performance status. Does our patient gain benefit from modified radical mastectomy, or radiofrequency for HFL? We prefer to continue on hormonal treatment and targeted therapy.

4. Conclusion

Due to the rising incidence of multiple primary malignancies, further studies should be done not only for better clinical evaluation and treatments but also for accurate determination of possible etiologies, pathogenesis, effective managements and screening programs.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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