

Case Report

Synchronous dual malignancy: a rare case report of carcinoma breast with carcinoma gall bladder

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ABSTRACT

Incidence of multiple primary cancers is reported to be between 0.18% to 17.2% in various studies. Occurrence of breast and gall bladder malignancy as synchronous malignancy is very rare. We are reporting one of such rare case. Our patient, a 64 years old lady had a unique presentation. She underwent laparoscopic cholecystectomy for a clinical diagnosis of cholelithiasis. Histopathology turned out to be adenocarcinoma of the gall bladder (stage II A). A clinical examination done at the time of presentation to our institute revealed suspicious thickening of the skin of the left breast and a subsequent tru-cut biopsy revealed infiltrating ductal carcinoma. Hormone receptor immunohistochemistry revealed Estrogen receptor (ER) negative Progesterone receptor (PR) negative and Her2neu negative tumour. Further evaluation revealed a widespread metastatic disease. She was treated with palliative radiotherapy, chemotherapy and zoledronate. She had an aggressive clinical course and succumbed to her illness within four months after diagnosis of dual malignancy. There is a high incidence of gall bladder carcinoma along the Gangetic belt of Northern India. Presence of dual malignancy with gall bladder carcinoma as one primary in these geographic location needs to be further explored for sporadic environmental factors or other genetic alterations as possible causative factors.

Keywords: Breast, Gall bladder, Synchronous malignancy

INTRODUCTION

The leading site of cancer in women worldwide and in India is breast with an incidence of 24.7 per 100,000 women.¹ The incidence of gallbladder carcinoma in India is very high in the northern Indo-Gangetic plains with an incidence of 10.1 per 100,000 for women when compared with that of south India.² Metastasis of carcinoma breast to gallbladder and vice versa have been reported in literature. But very few case reports of both malignancies occurring together have been reported till date.³ Management of such a case will depend upon the stage of individual cancer and the presence or absence of metastatic disease. We report a

case of synchronous dual malignancies of carcinoma breast with carcinoma gallbladder.

CASE REPORT

A 64-year-old postmenopausal lady presented with complains of abdominal pain of three months' duration. Ultrasound of the abdomen done at an outside centre showed multiple gall stones and she underwent laparoscopic cholecystectomy. Tissues sent for histopathological examination of the cholecystectomy specimen revealed adenocarcinoma of the gall bladder. The patient presented to our centre for further treatment

and completion surgery. Her clinical examination revealed a thickening of the skin of the left breast with peau d'orange appearance and retraction of the nipple (figure 1). Patient had multiple enlarged lymph nodes in the left axilla as well as an enlarged lymph node in the left supraclavicular region. General systemic examination was otherwise normal. Abdomen examination was unremarkable except for laparoscopy scar. A provisional diagnosis of carcinoma gallbladder stage II A (pT2aN0M0) with carcinoma left breast cT4bN3cMx was made as per the American joint committee on cancer (AJCC) staging manual 8th edition.⁴



Figure 1: Thickening of the skin of the left breast with peau d'orange appearance and retraction of nipple.

The patient was referred to the integrated breast clinic at our institute where a mammography was done. Mammography revealed diffuse trabecular thickening in the left breast with overlying skin thickening and a BIRADS 4 C lesion measuring 3.4x2.7 cm (figure 2). Ultrasound of the left axilla and neck showed multiple enlarged infiltrated lymph nodes in the left axilla, left infraclavicular and left supraclavicular region. A 18F-FDG whole body Positron emission tomography-Computed tomography (PET-CT) Scan was also done which revealed multiple sites of bony metastases at various vertebrae, pelvic bones, bilateral ribs, left scapula and right femur (figure 3). Core needle biopsy from the breast lesion revealed infiltrating ductal carcinoma.

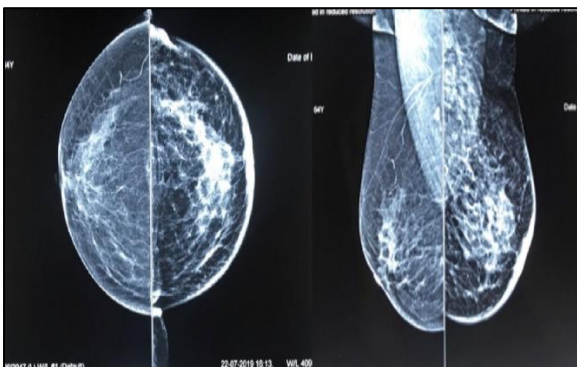


Figure 2: Mammography showing diffuse trabecular thickening in the left breast with overlying skin thickening.

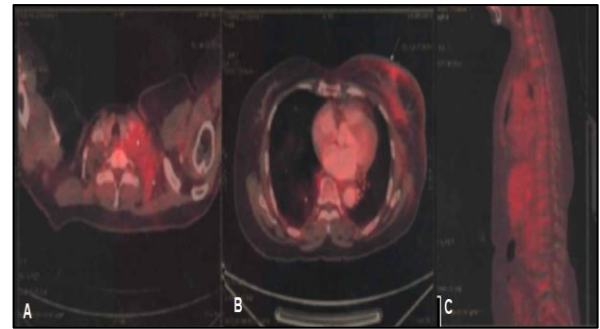


Figure 3: Whole body PET-CT Scan showing A: left supraclavicular metastasis B: Left breast thickening C: Diffuse skeletal metastases.

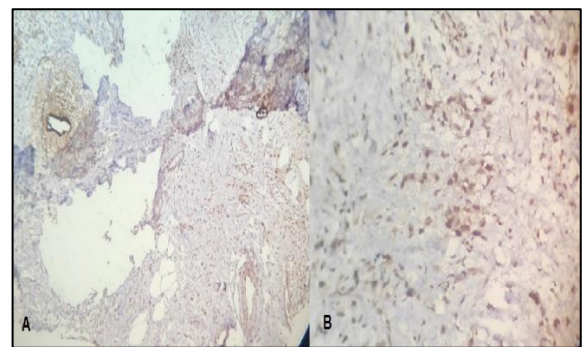


Figure 4: Breast specimen showing intense positivity with GCDFP stain. A. 4x magnification. B. At 40x magnification.

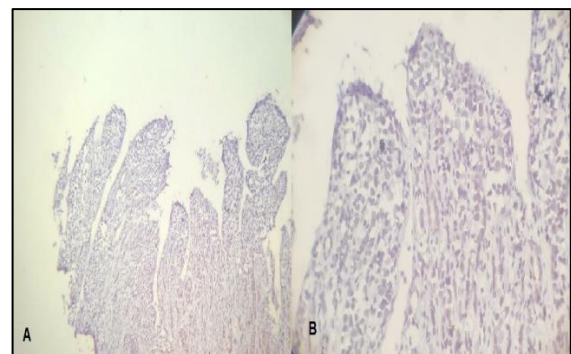


Figure 5: Gall bladder specimen showing non-specific negative staining with GCDFP. A. 10x magnification B. 40x magnification.

On immunohistochemistry (IHC), the breast specimen was negative for Estrogen receptor (ER), Progesterone receptor (PR) and HER-2 neu receptor. A slide and block review of the cholecystectomy specimen was also done at our pathology laboratory and was found to have moderately differentiated adenocarcinoma. On IHC, the gallbladder specimen was negative for ER, PR and HER-2 neu receptor. In order to distinguish between primary of gall bladder and metastatic disease from breast, Gross cystic disease fluid protein (GCDFP) stain was used.⁵ The breast specimen showed intensely positive staining with GCDFP suggesting primary tumor of the breast (figure 4). The

gallbladder specimen showed nonspecific negative uptake with GCDPF stain suggesting a primary adenocarcinoma of the gallbladder (Figure 5).

Initially a differential diagnosis of metastases of gallbladder to breast and vice versa or a synchronous dual malignancy of carcinoma breast with carcinoma gallbladder was considered. Despite the similar expression of ER, PR and HER-2 neu receptor on both the specimens, with the use of morphology and GCDPF stain we came to the final diagnosis of synchronous dual malignancy of carcinoma left breast and carcinoma gall bladder.

The patient received palliative radiation with 8 Gy to two vertebral sites C7 to T4 and T12-L5. She was started on Gemcitabine and Cisplatin based palliative chemotherapy. She received 1 cycle of Gemcitabine (1000 mg/m²) and Cisplatin (75 mg/m²) intravenous infusion on days 1 and 8. She came to us after 3 weeks with worsening of general condition, increase in size of the left supraclavicular node and severe pain. Patient was started on oral Morphine. Contrast enhanced CT (CECT) abdomen and thorax was done which revealed multiple new metastatic bony lesions in the pelvic bones, bilateral femur and vertebrae. She received 20 Gy/5 fractions to the left supraclavicular fossa and 4 Gy single fraction to the left scapula. Chemotherapy was then changed to Taxane-based chemotherapy. Patient is also started on monthly intravenous Zoledronic Acid. Following two cycles of intravenous Docetaxel the patient developed progressive disease with massive pleural effusion. Her general condition further deteriorated in spite of supportive measures and she succumbed to her illness within four months of diagnosis of double malignancy.

DISCUSSION

The occurrence of synchronous dual primary malignancy is not very common. As per various studies done in the recent past, the incidence of multiple primaries over all cancer sites ranges from 2.15% to as high as 17.2% worldwide.⁶ In India the incidence of double primary malignancies is 0.18% out of which around 19.51% are synchronous and 80.49% are metachronous.⁷

Table 1: Warren and Gates criteria for diagnosis of double primary malignancies.

1. Histological confirmation of malignancy in both 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 by at least five years.
3. Probability of one being the metastasis of the other must be excluded.

Double malignancies can be divided into two categories based of the time interval between the diagnosis of the two primaries viz., synchronous second primary and

metachronous second primary. Synchronous second primary is defined as index tumor and the second malignancy were diagnosed within 6 months of each other. Metachronous second primary is defined when the period between each diagnosis of the two primaries exceeds 6 months.⁸ We have used the Criteria for diagnosis of double primary malignancies proposed by Warren and Gates (table 1) to come to the final diagnosis of our patient as synchronous dual malignancy of carcinoma breast and carcinoma gallbladder.⁹

Management of such synchronous malignancy may depend on several factors like aggressiveness of the disease, stage of individual malignancies, whether the primary has been addressed with some other modalities like surgery or radiotherapy, intrinsic chemoresponsiveness of the tumour, presence of targetable molecular alterations, patient’s general condition etc. Following the final diagnosis of our patient, she was started on a chemotherapy regimen that was able to address both gall bladder and breast malignancy, but comparatively more effective in gall bladder carcinoma. This decision was done based on an assumption of aggressive nature of gall bladder malignancy. But she did not respond to this regimen and reported back after first cycle with a progressive disease in breast with severe pain in the supraclavicular region which forced us to change the chemotherapy regimen to Docetaxel. She failed to respond to this regimen also and succumbed to her illness.

High incidence of gall bladder malignancy is a major concern in the Gangetic belt of Northern India unlike the other parts of India. Management decisions in patients with multiple cancers become very difficult especially in those with cholangiocarcinoma as one primary which in itself is having an aggressive clinical course. Presence of dual malignancy with gall bladder carcinoma as one primary in these geographic location needs to be further explored for sporadic environmental factors or other genetic alterations as possible causative factors.

CONCLUSION

Dual malignancies present a challenge in terms of management as there is little evidence guiding the choice of treatment. Choice of treatment should take into account both the stage and histology of each malignancy in case of Synchronous dual primaries. The scenario at hand is further complicated, the etiology of which is potentially stretched across environmental factors and genetic alterations. More similar cases need to be reported and studied to understand the natural course and to formulate a plan of management which guides clinicians and best benefits such patients.

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