



Synchronous Early Breast Cancer and Locally Advanced Primary Bladder Adenocarcinoma

Sepideh Meshgi, Sahel Valadan Tahbaz, Hossein Yahyazadeh, Mahsa Mohammadzade, Abdollah Nasehi, Saadat Molanaei

Clinical Cancer Research Center, Milad General Hospital, Tehran, Iran.

ABSTRACT

Aim: Synchronous occurrence multifocal tumors across multiple tissues are common and mostly metastatic and sometimes include a small number of concurrent multiple primary tumors that are not metastatic poses so it is a difficult challenge to treatment, so we present a case of synchronous primary well differentiated adenocarcinoma of bladder and invasive ductal carcinoma of breast.

Case report: A 59-year-old female patient presented to urology department with the complaint of pain and hematuria. There was no relevant family history for all type of cancers. Clinical examination was normal. The patient had no history of tobacco using and any other cancer in the past. Through core needle biopsy, the patient was diagnosed with invasive ductal carcinoma of left breast. All sentinel lymph node of breast was sent to pathology and it revealed that the node is involved. Simultaneously, partial mastectomy was done for patient, and then axillary lymph node dissection has been done; six lymph nodes were removed and sent to the lab.

Discussion: A comorbid manifestation of breast and bladder carcinomas is rare, little similar case has been published so far. Synchronous primary cancers have rarely been reported, but it is believed that the incidence is rising. Prevention, making an early diagnosis and the treatment of multiple cancers will become even more important in the future.

Conclusion: It is important to present this case because of many literature have been reported cases of bladder metastasis of the breast, but we presents a concurrent primary breast and bladder cancer report.

Key Words: Synchronous Cancer, Bladder Tumor, Breast Tumor, Adenocarcinoma, Malignancies

INTRODUCTION

The incidence of breast cancer in the early stages concurrent with the primary bladder tumor has rarely occurred in the literature and research papers. Bladder cancer has the highest prevalence rate among the urologic cancers^{1,2}. Breast cancer is the most common malignant disease affecting women, after non-melanoma skin cancers, and the second reason for cause of death for cancer in women, mainly due to metastatic spread^{3,4}. Common areas for breast cancer metastatic are lung, bone, liver, lymph nodes, and skin but rarely spreads to other sites, such as urinary bladder and retroperitoneum⁴. For the first time, Avicenna, Iranian (Persian-Muslim) philosopher and physician, reported primary multiple tumors (PMTs) as a case with bilateral mammary

glands malignancies⁵. Billroth et al. described the phenomenon of multiple primary malignancies (MPC) in a single individual, in the late 19th century⁶. Warren and Gates's criteria define the necessary condition which tumors must fulfill to be included in the MPCs. The criteria consist of: each tumor should belong to a specific malignancy and they should not be the result of metastasis from another tumor⁷. MPCs are categorized to either metachronous and synchronous, which the second one is rather rare⁸. Concurrent association of two primary malignancies or appearance of the second one within 6 months would be called synchronous cancer⁹. Among many cancers, bladder cancer has the highest incidence rate among the urologic cancers⁸. We describe here an extremely rare case of synchronous double primary cancer involving the bladder and breast. Therefore, we

Corresponding Author:

Dr. Sahel Valadan Tahbaz, Clinical Cancer Research Center, Milad General Hospital, Tehran, Iran.

Tel: +98 9124805450; E-mail: s_valadan@ymail.com

ISSN: 2231-2196 (Print)

ISSN: 0975-5241 (Online)

Received: 19.02.2020

Revised: 02.04.2020

Accepted: 16.04.2020

report a remarkable case of completely synchronous primary bladder and breast cancer.

CASE REPORTS

A 59-year-old female patient presented to our urology department in Milad General Hospital, a part of Iran Social Security Organization, with the complaint of pain and hematuria. In urine analysis, RBC was found to be 25-30 units with trace protein, hyaline casts, and pus. There was no relevant family history for all type of cancers. Clinical examination was normal. The patient had no history of tobacco using and any other cancer in the past.

In the CT scan, tumor mass was confined to the bladder, and there was no lymphadenopathy in the pelvic (Figure. 1). The patient underwent transurethral resection (TUR). TUR results showed well differentiated adenocarcinoma (Figure 2.A) and no thickness of invasion was reported in pathology comments. In immunohistochemistry staining, which its findings were consistent that CK7, GATA3, ER, PR, HER-2, CD15, CA125, B-Catenin, and Vimentin were negative; CDX2 (Figure 2.B), CK20, and EMA were positive (Figure 2.C).

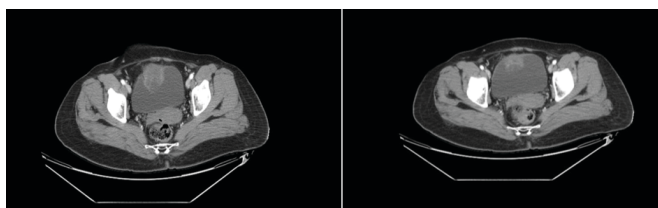


Figure 1: Bladder tumor mass was evident in the CT scan

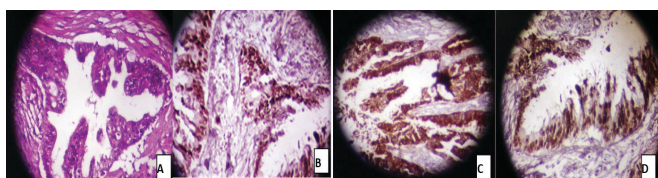


Figure 2: (A), The pathologic features of the bladder tumor (H&E stain, $\times 100$); (B), CDX2 biomarker in bladder tumor is positive (H&E stain, $\times 100$); (C), CK7 biomarker in bladder tumor is positive; (D), CK20 biomarker in bladder tumor is positive. The microphotograph showed well differentiated adenocarcinoma with bladder origin.

In checking of primary origin and for excluding metastatic bladder adenocarcinoma of gastrointestinal origin, after colonoscopy and endoscopy was conducted, so results confirmed that the malignancy didn't in gastrointestinal (GI) origin. (Figures 3A and 3B).

That period, the patient noticed a firm mass in her left breast. Mammography determined the existence of left breast mass (Figure 4).

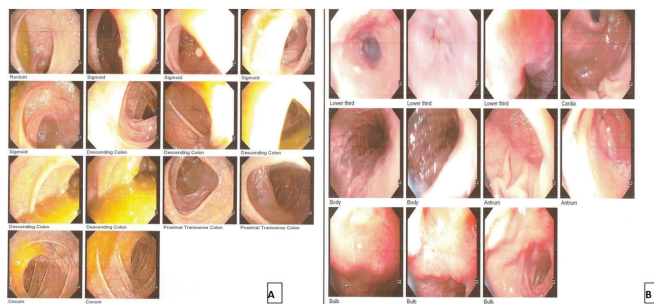


Figure 3: (A), Colonoscopy Results; (B), Endoscopy Results.

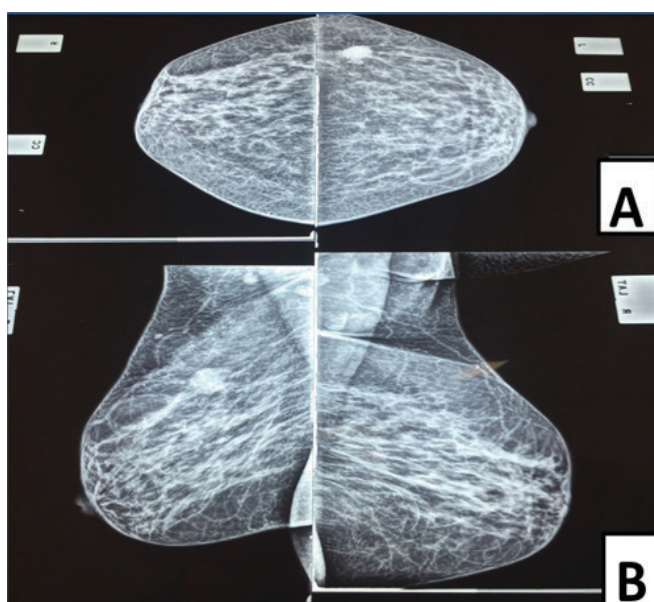


Figure 4: Mammography image, (A), Cranio-caudal view; (B), Mediolateral view. Mammogram showing nodular irregular homogeneous density present in left breast.

Through core needle biopsy, the patient was diagnosed with invasive ductal carcinoma of left breast. All sentinel lymph node of breast was sent to pathology and it revealed that the node is involved. Simultaneously, partial mastectomy was done for patient, and then axillary lymph node dissection has been done, six lymph nodes were removed and sent to the lab. According to laboratory reports, one of the nodes was involved and the tumor size was $2.5 \times 2 \times 2$ cm (T2). The TNM stage of breast tumor determined as pT2N1M0 (stage IIIA). That axillary lymph node was sent to the lab for immunohistochemistry examination. As a results of IHC tests; ER (Figure 5.B), PR were positives, and HER-2 was (+2) but the result of FISH test was negative. Ki67 was positive in 5% of cells.

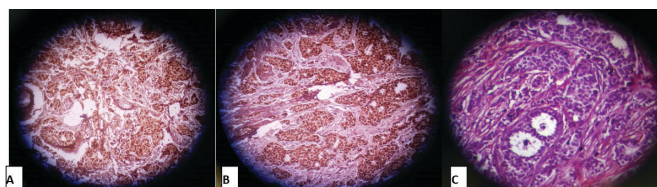


Figure 5: (A), The pathologic features of the breast tumor that ERpositive in breast tumor; (B), PRpositive in breast tumor; (C), Haematoxylin and eosin staining, x100 magnification of breast tumor. Histopathology slide with immunohistochemistry stain showing ductal carcinoma of breast cancer.

Finally, the patient was returned to urology department and partial cystectomy was done for her. Microscopic findings supported that she had well-differentiated adenocarcinoma and tumor was invaded to serosal layer and peripheral fat but all margins were free and no lymphadenopathy was performed. TNM stage of the bladder tumor was pT3NxM0.

Tumor marker tests indicated serum levels of CA15-3, CA125-ECL, CEA-ECL AFP- Tumor marker ,and Beta HCG which they were respectively 39.4 U/ml (High Level), 5.6 U/ml, 1.8 ng/ml, 4.5 IU/ml ,and <0.5 mlu/ml. As a double check, cystectomy samples were sent for IHC and the result was as before; CK7, CK20, CA125 and Vimentin were negative and EMA and CDX2 were positive. These findings confirmed the final diagnosis is primary bladder well differentiated adenocarcinoma so there is a synchronous primary bladder and breast cancer.

DISCUSSION

Characteristics of her disease met the Warren and Gates conditions; we reported her case as an MPC. By searching the databases a few similar cases, with synchronous bladder and breast cancer, were found. One of them was a 57-year-old male patient with triple simultaneous neoplasms including transitional cell carcinoma (TCC) of the urinary bladder, infiltrating ductal breast carcinoma, and squamous cell carcinoma (SCC) of the forehead skin, which was reported by Pastore et al. in 2013. The reports represent He was a farmer and chronic smoker, and his family history contains two relatives with malignancies; his father with rectal cancer and his sister who had kidney neoplasm. He was sent to the institute for hematuria. Ultrasound findings illustrated several bladder papillary lesions rooted from the left wall of the bladder, and cystoscopy results validate the primary findings of multiple bladder papillary lesions. Additional examinations including TURB and Later second histopathological tests revealed grade III papillary transitional cell carcinoma. IHC staining showed positive results for cytokeratin 7 and negative for cytokeratin 20 and GCDP-15. After his doctor noticed a hard mass and retraction on his left nipple, he

underwent radical mastectomy and dissection of the axillary lymph node. According to histopathological investigations, a grade III infiltrating ductal breast carcinoma (90% ER and 20% PR positive) and metastasis to axillary lymph nodes was diagnosed. Proliferative index, by ki-67 marker, was assessed 10%. Suggested treatments for his condition were cystoprostatectomy, pelvic lymphadenectomy, continent ileal urinary diversion and adjuvant therapy¹⁰. The next case was documented in an article in 2011 by William Makis. They described another unique patient with triple primary tumors. The case was a 66-year-old woman with a history of MS, diarrhea, and losing weight symptoms. No familial history was mentioned. Through F-18 FDG PET/CT scanning method, physicians discovered suspicious masses in her rectum, breast, and bladder, which after biopsy investigations; it became clear that they were three synchronous cancers. The patient underwent radiotherapy and anastrozole therapy. After three months, PET/CT was conducted. The result shows a reduction in rectum tumors' size, and breast masses were resolved (gone-demolished)^{10,11}.

CONCLUSION

In our case, dual primary malignancies were detected, breast and bladder. A comorbid manifestation of breast and bladder carcinomas is rare, and to the best of our knowledge, little similar case has been published so far. Synchronous primary cancers have rarely been reported, but it is believed that the incidence is rising. Prevention, making an early diagnosis and the treatment of multiple cancers will become even more important in the future. The study case report of synchronous malignancies may provide important evidence not only for clinical evaluation for future treatment of tumors, but also provide clues for the pathogenesis and the management of cancer usually for improvement of effective screening with the approach of treatment of patients effectively.

ACKNOWLEDGEMENTS

The work was supported by Milad General Hospital, Tehran, Iran.

Abbreviations

Primary multiple tumors (PMTs); Multiple primary malignancies (MPC); Transurethral resection (TUR); Gastrointestinal (GI); Transitional cell carcinoma (TCC); Squamous cell carcinoma (SCC).

Conflict of Interest Statement

Authors disclosed no conflicts of interests.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal that the patient understands that her name and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Funding

This project has been funded by Milad General Hospital.

REFERENCES

1. Mydlo JH, Gerstein M. Patients with urologic cancer and other nonurologic malignancies: analysis of a sample and review of the literature. *Urology*. Dec 2001;58(6):864-869.
2. Jiang W, Ding Y, Shen Y, et al. Identifying the clonal origin of synchronous multifocal tumors in the hepatobiliary and pancreatic system using multi-omic platforms. *Oncotarget*. Jan 17 2017;8(3):5016-5025.
3. Arjunan R, Kumar D, Kumar KV, Premalatha CS. Breast Cancer with Synchronous Renal Cell Carcinoma: A Rare Presentation. *J Clin Diagn Res*. Oct 2016;10(10):XD03-XD05.
4. Cormio L, Sanguedolce F, Di Fino G, et al. Asymptomatic bladder metastasis from breast cancer. *Case Rep Urol*. 2014;2014:672591.
5. Zhai C, Cai Y, Lou F, et al. Multiple Primary Malignant Tumors - A Clinical Analysis of 15,321 Patients with Malignancies at a Single Center in China. *J Cancer*. 2018;9(16):2795-2801.
6. Billroth T. [General surgical pathology and therapy. Guidance for students and physicians. Lecture]. *Khirurgiia (Mosk)*. Oct 1991(10):136-143.
7. Testori A, Cioffi U, De Simone M, et al. Multiple primary synchronous malignant tumors. *BMC Res Notes*. Nov 27 2015;8:730.
8. Komiyama S, Nishio E, Ichikawa R, et al. Asymptomatic synchronous quintuple primary cancers. *Gynecol Obstet Invest*. 2012;74(4):324-328.
9. Jiao F, Yao LJ, Zhou J, Hu H, Wang LW. Clinical features of multiple primary malignancies: a retrospective analysis of 72 Chinese patients. *Asian Pac J Cancer Prev*. 2014;15(1):331-334.
10. Pastore AL, Palleschi G, Autieri D, et al. Synchronous primary neoplasms of the bladder, skin and breast in a male patient: a case report. *World J Surg Oncol*. Oct 20 2013;11:282.
11. Makis W, Ciarallo A, Lisbona R. Three synchronous primary malignancies detected by F-18 FDG PET/CT: breast, rectal, and urothelial bladder carcinomas. *Clin Nucl Med*. Sep 2011;36(9):791-794.