Male Breast Cancer with Ureteral Metastasis: a case report

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Case report

Keywords: Male Breast Cancer, Ureteral Metastasis, Gene Test, Case Report

Posted Date: June 25th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-37173/v1>

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Version of Record: A version of this preprint was published at Annals of Palliative Medicine on July 1st, 2021. See the published version at <https://doi.org/10.21037/apm-20-2374>.

Abstract

Background: Breast cancer is rare in men and there is no report of male breast cancer (MBC) with ureteral metastasis. In this study, we report a special case of MBC with ureteral metastasis.

Case presentation: A 60-year-old man was diagnosed with breast cancer and lymph nodes metastasis. After surgery, chemotherapy and radiotherapy he was diagnosed with left arm metastasis. Then he received mass dissection and chemotherapy again. He was diagnosed with ureter metastasis because of hematuria. This patient took a Precitype gene test (immune index and PAM50) after several lines of treatment and the result indicated that this was a Luminal A subtype case, which was quite different from his immunohistochemical subtype. We adjusted his therapeutic regimen according to the genetic test but there was no obvious efficacy and he passed away five months later.

Conclusions: MBC patients with urinary symptoms should be considered for the possibility of metastasis although urinary metastasis in breast cancer is rare. We still need more research and evidence of treatment recommendations for MBC.

Introduction

Male breast cancer (MBC) is a rare disease with an incidence rate less than 1% of that of female breast cancer[1, 2]. On one hand, male patients usually have later onset of disease and more advanced stage than female patients. On the other hand, male patients have lower risk of death from breast cancer than comparable female patients[3]. MBC patients usually have different characteristic and distinct clinical features[4, 5]. However, only few published data were collected from small cohorts of male patients treated at single institutions and most treatment recommendations were from the results of clinical trials that enrolled only women[6], which results that evidence of MBC treatment guideline is insufficient. Common metastasis site of breast cancer includes axillary lymph nodes, lung, liver, bone and brain while ureteral metastasis is very rare[7]. Here we report a male breast cancer case with ureteral metastasis. During the treatment of this patient we suggested him to take a gene test and we modulated his therapy regiment according to his genomic test. We present the following case in accordance with the CARE reporting checklist.

Case Presentation

Lu XX, male, was 60 years old when diagnosed with breast cancer. He had a history of epilepsy and had been taking valproate orally for a long time and there was no family history of breast cancer or any other malignant tumors. He underwent left breast mass resection at local hospital in October 2016 and pathologic examination indicated breast cancer. Then he received surgery of breast mastectomy, axillary and supraclavicular lymph node dissection, following with 8 periods of chemotherapy and 25 times of radiotherapy. In August 2017, he found a mass on his right upper arm and doctors performed mass dissection surgery for him. After being confirmed of left arm metastasis, he came to our hospital for

further treatment. He received chemotherapy for 6 periods and began oral chemotherapy of capecitabine in April 2018. Unfortunately, the patient was diagnosed with ureter metastasis after middle ureter dissection and anastomosis because of hematuria and urinary obstruction. After that he also received double J tube insertion with percutaneous nephroscopy and cystostomy because of dysuria, severe urinary infection, persistent pain and obstruction of lower urinary tract. Genomic test was taken with his primary breast tumor tissue and the test result showed he was a Luminal A subtype case and RNA expression of HER-2 gene was positive. After MDT (Multiple Disciplinary Treatment) discussion we gave him endocrine therapy and anti-HER-2 target therapy with aromatase inhibitors, gonadotropin-releasing hormone (GnRH) analogue and trastuzumab because of his severe urinary infection and poor condition. However, it seemed that the treatment did not work and his condition was getting worse and worse and he passed away because of severe infection and multiple organ failure in April 2020. The whole therapeutic process of this case is detailed described and settled in Table 1.

Table 1
Therapeutic process of the case.

Time	Event/Treatment	Pathology or Gene Test
October 2016	Left breast mass resection. (Fig. 1)	Invasive ductal carcinoma (Grade III) ER (-); PR (-); HER-2 (2+); FISH (-); Ki-67 40% (+); E-cadherin (+); CK (+); CK7(+); Vimentin (-).
October 2016	Left breast mastectomy, axillary and supraclavicular lymph node dissection.	TNM stage: T4N3M0 (8/13 LN positive with supraclavicular LN metastasis). ER (-); PR (-); HER-2 (-); Ki-67 10% (+); CK (+); CK7(+).
November 2016 - July 2017	Chemotherapy: AC*4-T*4 (Adriamycin, iv; Cyclophosphamide, iv; Paclitaxel Liposome, iv) Radiotherapy (25 times at local region)	
August 2017	Mass dissection on left upper arm.	Breast ductal carcinoma metastasis
August 2017 - July 2018	Chemotherapy: NC*6-X*6 (Navelbine, iv; Carboplatin, iv; Capecitabine, po)	
July 2018	Hematuria	
March 2019	CT scan: right adrenal, bilateral anterior iliac lymph nodes, left gluteus maximus and ureter metastasis. (Fig. 2) Surgery of middle ureter dissection and anastomosis.	Breast cancer with ureter metastasis. ER (-); PR (-); HER-2 (1+); Ki-67 50% (+); CK (+); CK7(+). (Fig. 3)
March 2019 -June 2019	Chemotherapy: albumin-bound paclitaxel (iv)	Genetic (<i>BRCA1</i> , <i>BRCA2</i>) mutation test: negative
August 2019	Double J tube insertion with percutaneous nephroscopy at right ureter	
November 2019	Dysuria, pain in urination. Pelvic MR: retroperitoneal LN, bilateral pubic metastasis. Surgery of cystostomy.	Precitype gene test (immune index and PAM50): Luminal A subtype, RNA expression of HER-2 gene: positive

Time	Event/Treatment	Pathology or Gene Test
November 2019 -April 2020	Aromatase inhibitors plus gonadotropin-releasing hormone (GnRH) analogue and Trastuzumab	
April 2020	Death because of severe infection and multiple organ failure.	

Discussion And Conclusions

In this study, we introduced a special male breast cancer case with ureteral metastasis. His immunohistochemical character was rather different from the gene test. Although we adjusted his treatment regiment, this patient still had a poor result.

MBC is rather rare and the risk factors for MBC include demographic factors (black ethnicity, family history of breast cancer), genetic factors (germline genetic mutation, eg, *BRCA1*, *BRCA2*, *CHEK2*, *PALB2*), environmental factors and diseases associated with hyperestrogenism[6]. However, there was no family history of breast cancer in this case and the genetic test of BRCA mutation was negative. At the same time, no radiation exposure or other diseases reported as risk factors such as liver disease or testicular abnormalities or obesity in this patient. As a result, the exact cause of breast cancer in this patient was unclear and risk factors of MBC should be further studied in the future.

Research data shows that MBC risk has remained at a constant level over the past 40 years[3]. Compared with female patients, male patients have later onset and more advanced disease because of lacking of awareness of early signs of breast cancer and early detection by mammography screening[8]. Although overall survival of MBC is usually worse, male patients actually have a survival benefit after adjustment of life expectancy, age, time of diagnosis, stage and treatment[3, 9]. In our study, the patient was at advanced stage when diagnosed, which led to his poor prognosis. In a word, much improvement in outcome of MBC can be achieved by improving earlier detection such as awareness and promotion of breast self-examination and development of therapy guidelines.

Breast cancer commonly metastasizes to lymph nodes, lung, liver, bone or brain, and only few cases were reported metastasizing to other sites such as intestine or ureter, which may be easily misdiagnosed[7]. In this case, the patient developed a symptom of hematuria, which was considered urinary tract infection or primary tumors at first. After pathological examination and considering his past history of breast cancer, he was diagnosed with ureteral metastasis and received anti-tumor therapy again. This case reminds us that any patients with urinary symptoms as well as a history of breast cancer should not be easily ruled out of cancer metastasis. Further examinations or even pathologic biopsy is necessary for these patients.

Because there is still no certain evidence such as randomized clinical trials focusing on male breast cancer patients, treatment approaches are extrapolated from studies of treatment for women breast

cancer patients[10]. Adjuvant chemotherapy and HER-2 targeted therapy is suggested for MBC patients who are at substantial risk for recurrence and death since observational cohort studies have suggested improved survival among them[11, 12]. Although no randomized trials have evaluated the role of radiotherapy in men, observational studies have suggested a benefit in men with positive nodes after mastectomy[13, 14]. Endocrine therapy is an important part of male breast cancer management since more than 90% breast cancers in men are hormone-receptor-positive[15]. However, in our case, the patient was a triple negative case with ER (estrogen receptor) negative, PR (progesterone receptor) negative and HER-2 (human epidermal-growth-factor receptor 2) negative, which means that he could only benefit from chemotherapy and radiotherapy.

Genomic tests, such as Oncotype DX, or MammaPrint are increasingly used to evaluate the recurrence risk and prognosis for women with breast cancer and the likelihood that chemotherapy benefits[16]. Although these genomic tests are usually recommended for early stage patients to calculate a recurrence score and guide the choice of treatment, we still advised this patient to take a Precitype gene test (immune index and PAM50). This is a next generation RNA-Seq genomic test of 55 genes associating with ER related genes, HER-2 related genes, proliferation related genes and Basal related genes and 17 genes associated with immune genes. Genomic test indicated that this was a Luminal A case and the RNA expression of HER-2 was positive. Since his condition was bad and could not tolerate chemotherapy, we adjusted his therapy schedule with aromatase inhibitors plus gonadotropin-releasing hormone (GnRH) analogue and trastuzumab[17, 18]. However, it seemed that it did not work and his condition was getting poorer. Previous research had demonstrated that those patients would have worse prognosis if their PAM50 molecular subtyping is distinct with immunohistochemical subtyping[19], which may explain this patient's poor outcome to some extent. Genomic test such as Oncotype DX is increasingly being used in the management of MBC in clinical practice[20]. However, we need more long-term outcomes data to fully understand the implications of this practice.

We still know very little about MBC at present because of its rather low morbidity rate. More studies about the clinicopathological and immunohistochemical features of MBC should be conducted to build an evidence base that supports future treatment recommendations for this rare disease.

Abbreviations

MBC

Male breast cancer; ER:Estrogen receptor; PR:Progesterone receptor; HER-2:Human epidermal-growth-factor receptor 2; GnRH:Gonadotropin-releasing hormone; BRCA:Breast cancer susceptibility genes.

MDT:Multiple disciplinary treatment.

Declarations

Authors' contributions

Yanbo Chen and Jiannan Wu reviewed the literature and contributed to the manuscript drafting. Fengxi su and Tingting Hu were the patient's attending doctors and contributed to the manuscript drafting. Juanjuan Wang observed the pathological slices. All authors read and approved the manuscript.

Acknowledgement

We offer our thanks and respect to the patient and his families for their approvement of reporting this case for medical research.

Funding

This study was supported by the National natural science foundation of China (81672619).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CARE Checklist (2016) statement: The authors have read the CARE Checklist, and the manuscript was prepared and revised according to the CARE Checklist.

Consent for publication

This study was approved by the Medical Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (SYSEC-KY-KS-2019-152) and with written informed consent of the patient.

Competing interests

The authors declare that they have no competing interests.

References

1. Czene K, Bergqvist J, Hall P, Bergh J. How to treat male breast cancer. *Breast*. 2007;16(Suppl 2):147–54.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin*. 2018;68:7–30.
3. Miao H, Verkooijen HM, Chia KS, Bouchardy C, Pukkala E, Larønningen S, Mellemkjaer L, Czene K, Hartman M. Incidence and outcome of male breast cancer: an international population-based study. *J Clin Oncol*. 2011;29:4381–6.
4. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population-based comparison with female breast cancer. *J Clin Oncol*. 2010;28:232–9.
5. Cardoso F, Bartlett JMS, Slaets L, van Deurzen CHM, van Leeuwen-Stok E, Porter P, Linderholm B, Hedenfalk I, Schroder C, Martens J, et al. Characterization of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. *Ann Oncol*. 2018;29:405–17.
6. Giordano SH. Breast Cancer in Men. *N Engl J Med*. 2018;378:2311–20.
7. Xie J, Ying Y-Y, Xu B, Li Y, Zhang X, Li C. Metastasis pattern and prognosis of male breast cancer patients in US: a population-based study from SEER database. *Therapeutic Advances in Medical Oncology*. 2019;11:175883591988900.
8. Goss PE, Reid C, Pintilie M, Lim R, Miller N. Male breast carcinoma: a review of 229 patients who presented to the Princess Margaret Hospital during 40 years: 1955–1996. *Cancer*. 1999;85:629–39.
9. Scott-Conner CE, Jochimsen PR, Menck HR, Winchester DJ. An analysis of male and female breast cancer treatment and survival among demographically identical pairs of patients. *Surgery*. 1999;126:775–80. discussion 780 – 771.
10. Korde LA, Zujewski JA, Kamin L, Giordano S, Domchek S, Anderson WF, Bartlett JM, Gelmon K, Nahleh Z, Bergh J, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. *J Clin Oncol*. 2010;28:2114–22.
11. Patel HZ 2nd, Buzdar AU, Hortobagyi GN. Role of adjuvant chemotherapy in male breast cancer. *Cancer*. 1989;64:1583–5.
12. Hassett MJ, Somerfield MR, Baker ER, Cardoso F, Kansal KJ, Kwait DC, Plichta JK, Ricker C, Roshal A, Ruddy KJ, et al: Management of Male Breast Cancer: ASCO Guideline. *J Clin Oncol* 2020;JCO1903120.
13. Madden NA, Macdonald OK, Call JA, Schomas DA, Lee CM, Patel S. Radiotherapy and Male Breast Cancer: A Population-based Registry Analysis. *Am J Clin Oncol*. 2016;39:458–62.
14. Eggemann H, Ignatov A, Stabenow R, von Minckwitz G, Rohl FW, Hass P, Costa SD. Male breast cancer: 20-year survival data for post-mastectomy radiotherapy. *Breast Care (Basel)*. 2013;8:270–5.
15. Fentiman IS, Fourquet A, Hortobagyi GN. Male breast cancer. *The Lancet*. 2006;367:595–604.
16. Grenader T, Yerushalmi R, Tokar M, Fried G, Kaufman B, Peretz T, Geffen DB. The 21-gene recurrence score assay (Oncotype DX) in estrogen receptor-positive male breast cancer: experience in an Israeli

cohort. *Oncology*. 2014;87:1–6.

17. Eggemann H, Ignatov A, Smith BJ, Altmann U, von Minckwitz G, Rohl FW, Jahn M, Costa SD. Adjuvant therapy with tamoxifen compared to aromatase inhibitors for 257 male breast cancer patients. *Breast Cancer Res Treat*. 2013;137:465–70.
18. Zagouri F, Sergeantanis TN, Koutoulidis V, Sparber C, Steger GG, Dubsky P, Zografos GC, Psaltopoulou T, Gnant M, Dimopoulos MA, Bartsch R. Aromatase inhibitors with or without gonadotropin-releasing hormone analogue in metastatic male breast cancer: a case series. *Br J Cancer*. 2013;108:2259–63.
19. Kim HK, Park KH, Kim Y, Park SE, Lee HS, Lim SW, Cho JH, Kim JY, Lee JE, Ahn JS, et al. Discordance of the PAM50 Intrinsic Subtypes Compared with Immunohistochemistry-Based Surrogate in Breast Cancer Patients: Potential Implication of Genomic Alterations of Discordance. *Cancer Res Treat*. 2019;51:737–47.
20. Yadav S, Karam D, Bin Riaz I, Xie H, Durani U, Duma N, Giridhar KV, Hieken TJ, Boughey JC, Mutter RW, et al: Male breast cancer in the United States: Treatment patterns and prognostic factors in the 21st century. *Cancer* 2019.

Figures

Figure 1

Immunohistochemical staining of the tissue in ureter shows metastasis of breast cancer. A-D: HE staining shows atypical cells in ureter tissue. E: anti-HER-2 staining indicates HER-2 negative expression. F: anti-ki-67 staining shows about 50% of cancer cells positive expression.

Figure 2

Breast cancer with ureteral metastasis. The blue arrows indicate metastatic tumor zones and the red arrow indicates right dilated ureter.

Figure 3

Mammography of the patient. The red arrows indicate lesion on the of the right breast.

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