

## Case Report

# Successful use of bevacizumb and paclitaxel in a male breast cancer with liver metastases

Du-Ping Huang<sup>1</sup>, Xiao-He Ye<sup>2</sup>, Chun Jin<sup>1</sup>

<sup>1</sup>Department of Oncology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, China;

<sup>2</sup>Department of Radiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, China

Received July 31, 2014; Accepted August 26, 2014; Epub September 15, 2014; Published September 30, 2014

**Abstract:** Breast cancer in men is a rare cancer manifestation. In this article we report a case of male breast cancer with liver metastases, which showed a good response to a combined treatment of bevacizumb and paclitaxel, suggesting a useful option for the first-line treatment of patients with recurrent HER2-negative male breast cancer. And further assessment in a randomized clinical trial is needed.

**Keywords:** Male breast cancer, bevacizumb, liver metastases

A 72 years old man, was admitted with the complaint of a left breast lump that was noticed 5 weeks before, noted bloody discharge from the nipple. In the left breast, a 3.0 cm retro-mammillary mobile tumor was palpable. Ultrasound showed a tumor of 35 mm × 21 mm × 13 mm with irregular margins. While the initial CT scan of the chest, liver, abdomen, and pelvis was normal.

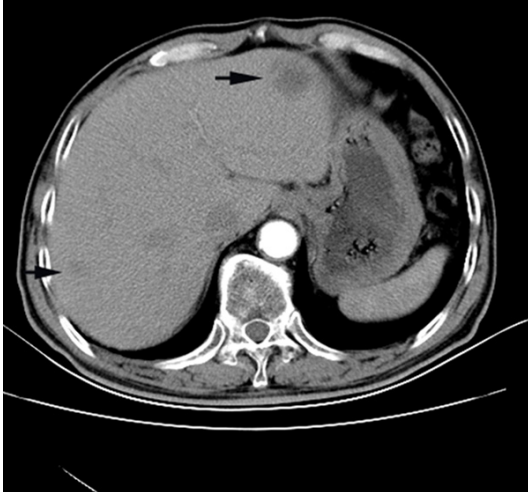
A modified radical mastectomy including lymph node dissection was performed on the left side. The final pathology revealed an invasive ductal carcinoma that was both estrogen receptor-positive (ER) (+) and progesterone receptor-positive (PR) (+), with a HER-2 -negative (IHC). A total of 4 out of 12 axillary lymph nodes were positive. The patient received 6 cycles of adjuvant TEC chemotherapy and adjuvant radiation. Afterwards, adjuvant endocrine therapy with 20 mg tamoxifen daily. And following-up examinations were conducted regularly. However, after about 15 months, multiple liver metastases were detected by a follow-up CT scan (**Figure 1**). The patient underwent percutaneous ultrasound-guided core biopsy of the liver tumors. Biopsy specimens showed the same pathological characteristics: metastatic invasive ductal carcinoma, ER (+), PR (+), and HER-2 (-). These findings confirmed the diagnosis as male breast cancer with liver metastasis.

To combat these, Tamoxifen was then replaced by the systemic treatment with Bevacizumb (10 mg/kg IV days 1 & 15) and Paclitaxel (90 mg/m<sup>2</sup> by 1 h IV days 1, 8, & 15). No severe adverse events above grade 3 were noted, and the patient was able to maintain a high quality of life between the combination treatments.

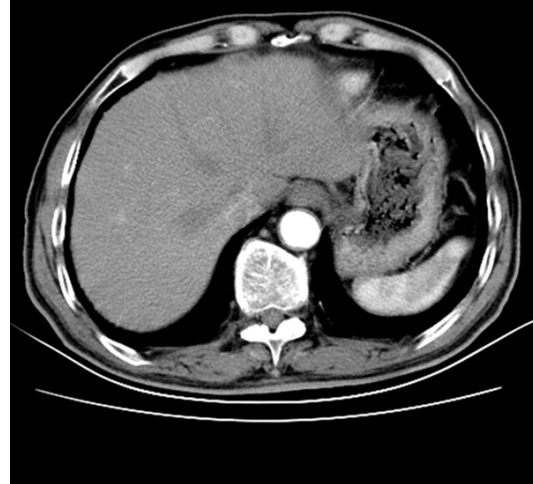
After 3 months, a follow-up CT scan was obtained (**Figure 2**). It showed that the metastatic liver tumor had completely disappeared. Subsequently, he continued with chemotherapy for 6 months, with repeat CT scans showed no evidence of tumor metastasis. However, because of coronary heart disease and hematologic toxicity, the patient finally refused further treatment. And he died for progression of disease 17 months later since the combination therapy started.

## Discussion

Male breast cancer is a rare disease, and researchers have focused relatively little attention on male breast cancer compared with female breast cancer [1, 2]. As a consequence, male breast cancer is often recognized later, and most patients present at an advanced clinical stage [3, 4]. However, survival is comparable to that in matched female patients [5]. Referring to systemic treatment in male breast



**Figure 1.** Baseline computed tomography scan showing multiple liver metastases (arrow).



**Figure 2.** Three months after the initial treatment with bevacizumab and paclitaxel, showing the disappearance of the tumor.

cancer, no data from clinical trials are available yet, treatment standards for men have generally been extrapolated from the enormous literature and clinical experience in women [6]. Bevacizumab is a humanized monoclonal antibody. And its main action is the inhibition of the function of vascular endothelial growth factor in the treatment of metastatic breast cancer [7, 8]. Several randomized phase III trials demonstrated significantly improved progression-free survival (PFS) and response rates (RRs) when bevacizumab was combined with taxane-based therapy as first-line therapy for locally recurrent or metastatic breast cancer [9-13]. However, after bevacizumab was granted “accelerated” approval by the US Food and Drug Administration (FDA) in 2008, in combination with weekly paclitaxel for the first-line treatment of HER2-negative metastatic female breast cancer (MBC), the FDA removed the MBC indication from bevacizumab in December 2010. In its decision, the FDA cited primarily safety concerns and that the risks that bevacizumab presented to patients with MBC outweighed any benefit in prolonging PFS. This decision was unexpected in the oncology community and remains controversial. However, available phase III clinical trials in patients with metastatic breast cancer, reveals that plus paclitaxel as first-line therapy had a generally acceptable tolerability profile [9, 13-15]. And the overall incidence of these toxicities was no higher than those found in patients with several types of advanced cancer, including colorectal cancer, lung cancer and renal cell cancer [16-19]. And

our case report showed the similar safety profile.

In the other hand, European regulatory authorities made a different conclusion compare with the FDA, and bevacizumab continues to be an accepted option for MBC treatment [20]. It is necessary to identify possible predictive biomarkers for anti-angiogenic therapy would translate into seeing a much larger therapeutic effect of the addition of bevacizumab to paclitaxel combination therapy.

Moreover, the increase in PFS with bevacizumab appears the greatest in combination with paclitaxel [21]. Therefore, The NCCN Panel has listed bevacizumab with paclitaxel as an option for treatment of patients with HER2-negative metastatic breast cancer.

However, there are no data on the efficacy of bevacizumab plus paclitaxel for male breast cancer with liver metastases. Applying a similar approach, we present this rare case of advanced male breast cancer that showed a good response to bevacizumab and paclitaxel therapy. Our results are generally consistent with those from the first-line bevacizumab randomized trials in a patient population that more closely mirrors patients treated in general oncology practice [11, 13, 15]. Indicating that combination therapy with bevacizumab and paclitaxel was a useful treatment of recurrent HER2-negative male breast cancer. We are

aware of no other anecdotal report of a similar case, although speculative, the results of our report with bevacizumab based on the PFS advantage may be instructive and warrant further assessment in a randomized clinical trial.

In conclusion, bevacizumab administered in combination with paclitaxel may be considered as an option for the first-line treatment of patients with recurrent HER2-negative male breast cancer.

### Acknowledgements

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Chun Jin, Department of Oncology, The First Affiliated Hospital of Wenzhou Medical University, No. 2, Fu Xue Road, Wenzhou 325000, China. Tel: 86-577-88078236; Fax: 86-577-88069555; E-mail: 13989765788@163.com

### References

- [1] Contractor KB, Kaur K, Rodrigues GS, Kulkarni DM, Singhal H. Male breast cancer: is the scenario changing. *World J Surg Oncol* 2008; 6: 58.
- [2] White J, Kearins O, Dodwell D, Horgan K, Hanby AM, Speirs V. Male breast carcinoma: increased awareness needed. *Breast Cancer Res* 2011; 13: 219.
- [3] Gnerlich JL, Deshpande AD, Jeffe DB, Seelam S, Kimbunde E, Margenthaler JA. Poorer survival outcomes for male breast cancer compared with female breast cancer may be attributable to in-stage migration. *Ann Surg Oncol* 2011; 18: 1837-1844.
- [4] Yildirim E, Berberoglu U. Male breast cancer: a 22-year experience. *Eur J Surg Oncol* 1998; 24: 548-552.
- [5] Foerster R, Foerster FG, Wulff V, Schubotz B, Baaske D, Wolfgarten M, Kuhn WC, Rudlowski C. Matched-pair analysis of patients with female and male breast cancer: a comparative analysis. *BMC Cancer* 2011; 11: 335.
- [6] Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. *Ann Oncol* 2013; 24: 1434-1443.
- [7] Wang Y, Fei D, Vanderlaan M, Song A. Biological activity of bevacizumab, a humanized anti-VEGF antibody in vitro. *Angiogenesis* 2004; 7: 335-345.
- [8] Presta LG, Chen H, O'Connor SJ, Chisholm V, Meng YG, Krummen L, Winkler M, Ferrara N. Humanization of an anti-vascular endothelial growth factor monoclonal antibody for the therapy of solid tumors and other disorders. *Cancer Res* 1997; 57: 4593-4599.
- [9] Miller K, Wang M, Gralow J, Dickler M, Cobleigh M, Perez EA, Shenkier T, Cella D, Davidson NE. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. *N Engl J Med* 2007; 357: 2666-2676.
- [10] Miles DW, Chan A, Dirix LY, Cortes J, Pivot X, Tomczak P, Delozier T, Sohn JH, Provencher L, Puglisi F. Phase III study of bevacizumab plus docetaxel compared with placebo plus docetaxel for the first-line treatment of human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol* 2010; 28: 3239-3247.
- [11] Gray R, Bhattacharya S, Bowden C, Miller K, Comis RL. Independent review of E2100: a phase III trial of bevacizumab plus paclitaxel versus paclitaxel in women with metastatic breast cancer. *J Clin Oncol* 2009; 27: 4966-4972.
- [12] Fountzilas G, Kourea HP, Bobos M, Televantou D, Kotoula V, Papadimitriou C, Papazisis KT, Timotheadou E, Efstratiou I, Koutras A, Penteroudakis G, Christodoulou C, Aravatinos G, Miliaras D, Petraki K, Papandreou CN, Papakostas P, Bafaloukos D, Repana D, Razis E, Pectasides D, Dimopoulos AM. Paclitaxel and bevacizumab as first line combined treatment in patients with metastatic breast cancer: the Hellenic Cooperative Oncology Group experience with biological marker evaluation. *Anti-cancer Res* 2011; 31: 3007-3018.
- [13] Robert NJ, Dieras V, Glaspy J, Brufsky AM, Bondarenko I, Lipatov ON, Perez EA, Yardley DA, Chan SY, Zhou X, Phan SC, O'Shaughnessy J. RIBBON-1: randomized, double-blind, placebo-controlled, phase III trial of chemotherapy with or without bevacizumab for first-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer. *J Clin Oncol* 2011; 29: 1252-1260.
- [14] Cella D, Wang M, Wagner L, Miller K. Survival-adjusted health-related quality of life (HRQL) among patients with metastatic breast cancer receiving paclitaxel plus bevacizumab versus paclitaxel alone: results from Eastern Cooperative Oncology Group Study 2100 (E2100). *Breast Cancer Res Treat* 2011; 130: 855-861.
- [15] Biganzoli L, Di Vincenzo E, Jiang Z, Lichinitser M, Shen Z, Delva R, Bogdanova N, Vivanco GL, Chen Z, Cheng Y, Just M, Espié M, Vinholes J, Hamm C, Crivellari D, Chmielowska E, Semi-

## Bevacizumab and paclitaxel in male breast cancer

- glazov V, Dalenc F, Smith I. First-line bevacizumab-containing therapy for breast cancer: results in patients aged  $\geq 70$  years treated in the ATHENA study. *Ann Oncol* 2012; 23: 111-118.
- [16] de Gramont A, Van Cutsem E. Investigating the potential of bevacizumab in other indications: metastatic renal cell, non-small cell lung, pancreatic and breast cancer. *Oncology* 2005; 69 Suppl 3: 46-56.
- [17] Hurwitz H, Fehrenbacher L, Novotny W, Cartwright T, Hainsworth J, Heim W, Berlin J, Baron A, Griffing S, Holmgren E, Ferrara N, Fyfe G, Rogers B, Ross R, Kabbinavar F. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *N Engl J Med* 2004; 350: 2335-2342.
- [18] Escudier B, Pluzanska A, Koralewski P, Ravaud A, Bracarda S, Szczylak C, Chevreau C, Filippek M, Melichar B, Bajetta E, Bajetta E, Gorbunova V, Bay JO, Bodrogi I, Jagiello-Gruszfeld A, Moore N; AVOREN Trial investigators. Bevacizumab plus interferon alfa-2a for treatment of metastatic renal cell carcinoma: a randomised, double-blind phase III trial. *Lancet* 2007; 370: 2103-2111.
- [19] Sandler A, Gray R, Perry MC, Brahmer J, Schiller JH, Dowlati A, Lilienbaum R, Johnson DH. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. *N Engl J Med* 2006; 355: 2542-2550.
- [20] Montero AJ, Escobar M, Lopes G, Gluck S, Vogel C. Bevacizumab in the treatment of metastatic breast cancer: friend or foe? *Curr Oncol Rep* 2012; 14: 1-11.
- [21] Yanagisawa M, Yorozu K, Kurasawa M, Nakano K, Furugaki K, Yamashita Y, Mori K, Fujimoto-Ouchi K. Bevacizumab improves the delivery and efficacy of paclitaxel. *Anticancer Drugs* 2010; 21: 687-694.