Breast cancer in patients with sickle cell disease can be treated safely with weekly paclitaxel

Aysha S. Al Zaman, *MBBS, MS (UK).*

ABSTRACT

تعد أورام الثدي أكثر الأورام السرطانية شيوعاً لدى الأناث بالرغم من تعدد وسائل العلاج المتوفرة حالياً وخاصة الأدوية الكيميائية التي بالإضافة إلى فعاليتها تعتبر بشكل عام آمنة من حيث الأعراض الجانبية حدة وخطورة ولكن ومع ذلك إلى الآن لم تتوفر أي دراسات أو تقارير عما إذا كانت هذه الأدوية آمنة للاستخدام لعلاج سرطان الثدي في شريحة حساسة من المجتمع وهم المصابين بمرض فقر الدم المنجلي. والذين هم أكثرعرضة من غيرهم للاصابة بمضاعفات العلاج الكيميائي كفقدان المناعة والالتهابات الناتجة عن ذلك بالإضافة إلى التعرض لنوبات السكر. نستعرض هنا حالة مصابة بفقر الدم النمجلي تبلغ من العمر 39 عام تم تشخيصها بورم خبيث في الثدي الأيمن وفي مرحلة متقدمة من المرض حيث قد امتد الورم الى الكبد والعظام. وبناء عليه تم اخضاع المريضة لجرعات العلاج الكيميائي المعروف بباكليتاكسيل (الجدول الأسبوعي) المستخدم في مثل هذه الحالات 80 ملغ/متر مربع في اليوم الأول، والثامن، والخامس عشر كل 28 يوم الجرعة القياسية المستخدمة لعلاج سرطان الثدي. تمكنت المريضة من تلقي جرعات العلاج كاملة بانتظام دون الحاجة إلى حذف أو تقليل أي جرعة ودون حدوث أي مضاعفات خطيرة. كانت الأعراض الرئيسة الجانبية هي التهاب الأغشية المخاطية وغثيان، كما لم يتسبب الدواء في حدوث أي نوبات ألم أو تكسر في الدم مما يثبت أن جرعات الباكليتلكسيل الأسبوعية دواء فعال وآمن لعلاج سرطان الثدي في المرضى المصابين بفقر الدم المنجلي.

Breast cancer is the most common malignancy among females; nevertheless, so far no data is available in the literature on the safety of oncological treatments in patients with sickle cell disease (SCD). Here we report a case of a 39-year-woman with SCD who presented with metastatic breast cancer, and was treated accordingly with weekly paclitaxel 80 mg/m^2 day one, 8, and 15 every 28 days as a standard regimen for metastatic breast cancer. She managed to complete the full course of chemotherapy (18 doses) of weekly treatment without any dose reductions or delays. The main side effects were: grade 1 nausea; and grade 2 mucositis. However, surprisingly there was no episode of febrile neutropenia, anemia, or thrombocytopenia. Moreover, she had no vaso-occlusive crisis while on chemotherapy. Therefore, weekly paclitaxel is both safe and well tolerated in SCD patients with breast cancer.

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From the Department of Oncology & Hematology, Salmaniya Medical Complex, Manama, Bahrain.

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Address correspondence and reprint request to: Dr. Aysha S. Al Zaman, Department of Oncology & Hematology, Salmaniya Medical Complex, PO Box 21853, Manama, Bahrain. Tel. +973 (1) 7284183. Fax. +973 (1) 7284192. E-mail: AZaman@health.gov.bh

Breast cancer is the most common malignancy among females, and is the leading cause of cancer related deaths in the general population. However, the incidence of malignancy, and in particular breast cancer in patients with sickle cell diseases (SCDs) is not well known. Most of our knowledge comes either from limited single institutional retrospective studies, or from several small cases series.[1-3] The result of those studies have demonstrated that SCD provided no increased risk of developing cancer, but also conferred no protection, except in SCD patient who are on hydroxyurea or underwent bone marrow transplant.[4-7] Treatment of breast cancer in patients with SCD represents unique challenges for the clinician. This is attributed to increased incidence of serious complication with the administration of some hormonal and chemotherapy drugs seen in SCD population compared to normal individuals. For instance, the risk of thromboembolism and cardio toxicity were greater in breast cancer patients with SCD who were treated with Tamoxifen and anthracyclin.[3] Moreover, Capecitabine was reported to precipitate vaso-occlusive crisis.[8] Taxanes are considered to be cornerstone chemotherapeutic drugs used to treat breast cancer both the adjuvant and metastatic setting, either as single agents or in combination. Single agent weekly paclitaxel is widely used as a standard of care

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for metastatic breast cancer, however, the safety and tolerability of this chemotherapy protocol is not well established in SCD patients. Here, we present a case of a sickle cell patient who was diagnosed with breast cancer, and was treated successfully with Taxol-based chemotherapy in our institution.

Case Report. A 39-year-old-lady with a known case of SCD presented with self-detected slowly growing lump in the upper outer quadrant of the right breast, which was associated more recently with pain and discoloration of the overlying skin. She was neither on hydroxyurea, nor underwent bone marrow transplant, and had infrequent hospitalization due to SCD crisis. She had menarche at age of 12, and had her first child at age of 28. Her family history was negative for malignancy. On physical examination, 2 ill-defined masses were identified in the right outer quadrant of the right breast with inflammation of the overlying skin. On ultrasound examination of the right breast (**Figure 1**) 2 ill-defined hypo-echoic mass lesions of approximately 2.6 cm x 1.5 cm and 1.3 cm x 1.2 cm highly suspicious of malignancy were noted in the right breast, and true cut biopsy was consistent with invasive ductal carcinoma of the breast. The immunohistochemistry showed the tumor cells to be progesterone receptor (PR) and human epidermal growth factor receptor (Her-2) negative with minimal ER positivity. Metastatic work out showed multiple lung and bone lesion, and therefore was staged as T4NXM1 multifocal breast cancer. Accordingly, she was started on weekly paclitaxel at a dose of 80mg/m^2 day one, 8 and 15 every 28 days. Paclitaxel was administered by one-hour intravenous infusion, and was preceded by a short premedication, consisting of hydrocortisone 100 mg, ranitidine 50 mg, and diphenhydramine 50 mg, which was given prior to each dose of paclitaxel. She has tolerated the chemotherapy well without any dose reductions or delays. The main side effects were: grade 1 nausea; and grade 2 mucositis; however, none of the treatments were complicated by febrile neutropenia, anemia, or thrombocytopenia, and patient never required any granulocyte colony stimulating factor (G-CSF) support. More over, other serious side effects, which is associated with taxanes like hypersensitivity and peripheral neuropathy were not reported in this patient. Interestingly, she did not have any episodes of vaso-occlusive crisis while on chemotherapy. At the end of the treatment, she had both clinical and radiological responses as manifested by complete disappearance of the breast lumps and overlying skin changes, as well as reduction in the size of liver and lung metastasis.

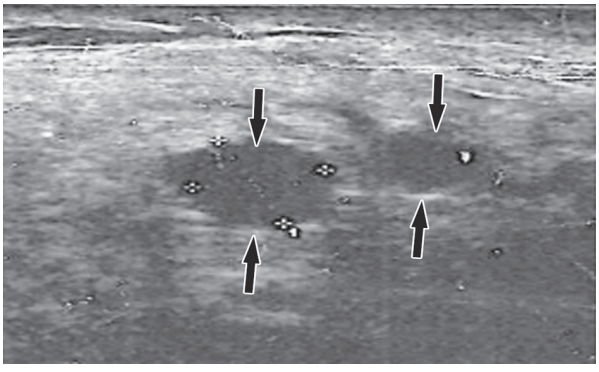

Figure 1 - Ultrasound of right breast showing multifocal breast carcinoma with 2 ill-defined hypo-echoic mass lesions in the right upper quadrant (arrows).

Discussion. Treatment of breast cancer in patients with SCD represents a real challenge as the guidelines for oncological treatments of SCD patients with breast cancer (surgical, chemotherapy, or radiation) are lacking. Unfortunately, so far there is no available data on the exact incidence, treatment, and safety of chemotherapy for this group of patients, except for a literature review by Schultz and Ware,[2] which reported a collection of 47 cases of malignancy in SCD over the past 50 years. Of these, 7 cases were breast cancers, but unfortunately there was no elaboration regarding the type of treatment administered, and the safety and tolerability of such treatments. The SCD patients are prone to develop vaso-occlusive, hemolytic and aplastic crisis, as well as sepsis more than normal individuals. This is often precipitated by dehydration and infections. Taxanes including paclitaxel and docetaxel are common drugs used in clinical practice to treat breast cancer, which are considered to be moderately emetogenic, and are not uncommonly associated with immunosuppression Therefore, chemotherapy is anticipated to be poorly tolerated and associated with greater toxicity in patients with SCD. More over, SCD patients may have pre-existing hepatic or renal impairment, and therefore, may have impaired drug metabolism and excretion resulting in more anticipated drug related toxicities. However, we have shown that paclitaxel when administered on weekly bases is well tolerated and safe in SCD patients, and neither carries any increased risk for neutropenia, nor requires additional support with G-CSF or transfusions. This further illustrates that weekly administration of paclitaxel, which has already demonstrated sustained efficacy manifested as increase in response rate (RR) and time to progression (TTP) together with a more favorable toxicity profile (for example, less myelotoxicity) than the 3-weekly

administration[9] in normal individuals can be safely applied to patients with SCD. Weekly paclitaxel was not complicated by exacerbation of sickle cell crisis, a serious complication reported with some other chemotherapeutic agents like capecitabine.[8] This could be due to favorable effect on fetal hemoglobin (HbF) level as seen with hydroxyurea. The HbF interferes with the polymerization of sickle hemoglobin (HbS) and hence, increases in HbF production could decrease the severity of disease in subjects with sickle cell anemia.[10]

The reason why different chemotherapeutic drugs has different effects on precipitation or protection against painful crisis can be explained further by the fact that individual chemotherapeutic drugs have different chemical structures and component, some of which are blamed to directly precipitate painful crisis. Another important mechanism might be polymorphisms in genes regulating HbF expression, individual drugs metabolism and erythroid progenitor proliferation. Therefore, ultimately HbF levels may vary in different individuals even with the same drug.[10]

In conclusion, weekly paclitaxel protocol is both safe and well tolerated, as well as effective for treating breast cancer in patients with SCD. However, the oncological community must report all cases of breast cancer in patients with SCD that have been treated successfully with various anticancer agents aiming to create a registry of such cases. This would be a very useful tool for clinicians in the choice of a safe treatment regimen for such critical group of patients.

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