Clinical Case Report

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Treatment of a patient with breast cancer and glucose 6-phosphate dehydrogenase deficiency

A case report

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Abstract

Rationale: Glucose 6-phosphate dehydrogenase (G6PD) deficiency is the most common enzymatic disorder of red blood cells that cause hemolytic anemia. Some anticancer drugs are reported to trigger oxidative stress; however, events of hemolysis are rarely discussed in patients with G6PD deficiency required oncologic treatments.

Patient concerns: Here we reported a young woman with G6PD deficiency safely undergoing breast cancer treatment.

Diagnosis: A 29-year-old patient was diagnosed with advanced cancer of the right breast with tumors positive for hormone receptor and human epidermal growth factor receptor 2.

Interventions: The patient received chemotherapy with doxorubicin, cyclophosphamide, and docetaxel. During the administration of docetaxel, trastuzumab was concurrently administered and was continued after the completion of docetaxel. The patient underwent adjuvant radiotherapy; meanwhile, tamoxifen was administered as adjuvant endocrine treatment.

Outcomes: The treatment process was smooth. There was no evidence of hemolytic anemia. Except for hot flushes, the patient lives without remarkable side effects from ongoing or previous treatments.

Lessons: Some patients have both G6PD deficiency and malignancy in a geographic area with relatively high incidence of the enzymatic disorder and certain types of cancer. We suggest that our report can contribute to the concern regarding the safety of patients with G6PD deficiency undergoing cancer treatment.

Abbreviations: G6PD = glucose 6-phosphate dehydrogenase, HER2 = human epidermal growth factor receptor 2.

Keywords: breast cancer, doxorubicin, glucose 6-phosphate dehydrogenase deficiency, hemolysis, tamoxifen

1. Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a genetic and inherited disorder. The defective G6PD gene located on the X chromosome induces hemolysis when red blood cells are exposed to oxidative stress. This disease affects millions of people and occurs worldwide.[1,2] Medication such as antibiotics or urate oxidase is well known to cause hemolysis in patients with G6PD deficiency. Moreover, some chemotherapy drugs can induce oxidative stress[3] and theoretically increase the risk of hemolysis. However, less information is available regarding the safety of anticancer drugs in this population. Only 1 report mentions a patient with G6PD deficiency safely receiving docetaxel plus cyclophosphamide for breast cancer.[4] Here we report the case of a young woman with breast cancer having G6PD deficiency who is undergoing chemotherapy, anti-human epidermal growth factor receptor 2 (HER2)-targeted therapy, and endocrine therapy. No evidence of hemolysis has been detected during treatment.

2. Case report

In October 2017, a 29-year-old woman presented with a lump in her right breast that persisted for more than 1 year. Her breast tumor gradually enlarged with nipple invasion and ulcer. Cancer in the right breast was diagnosed after biopsy. The pathology report revealed invasive ductal carcinoma with histologic grade 2. Tumor cells were positive for estrogen receptor, progesterone receptor, and HER2 in the immunohistochemistry staining. Mammography, breast sonography, computed tomography of the chest, and bone scan were used for accurate tumor-node-metastasis staging. The clinical stage was T4bN1M0. The patient reported having G6PD deficiency but no other systemic or inherited disease. Serum G6PD level was examined (3.5 U/g hemoglobin; normal range 6.4–12.9 U/g), and the deficiency was confirmed. Her father also has G6PD deficiency, but her mother, sister, and brother do not have the disease. The treatment plan included surgery followed by adjuvant chemotherapy, anti-HER2-targeted therapy, endocrine therapy, and radiotherapy.

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The patient received modified radical mastectomy of the right breast in November 2017, and the pathological stage was pT4bN1aM0, pStage IIIB. She had a smooth recovery after the surgery.

The patient belonged to the high-risk population of developing relapsed disease owing to young age, advanced tumor size, metastasis in axillary lymph nodes, and overexpression of HER2. Therefore, it was recommended that she receive sequential adjuvant chemotherapy with a regimen of doxorubicin plus cyclophosphamide followed by triweekly docetaxel. Adjuvant targeted therapy with trastuzumab would be initiated with docetaxel and lasted for 1 year. In addition, endocrine treatment with tamoxifen would be prescribed after completion of adjuvant chemotherapy. Before initiating adjuvant treatment, literature review was performed to determine the risk of hemolysis. Although hemolysis could be induced during oxidative stress in patients with G6PD deficiency, there was no direct correlation between hemolysis in patients with G6PD deficiency and anticancer treatment. The patient was informed about the uncertain risk of hemolysis while using anthracycline and tamoxifen. Considering the high risk of breast cancer recurrence, the patient decided to receive standard treatments for her disease after evaluating the pros and cons. The first cycle of chemotherapy with the regimen of doxorubicin (60 mg/m^2) plus cyclophosphamide (600 mg/m^2) was administered 3 months after initial diagnosis. The patient had an uneventful recovery. Her hemogram and biochemistry data 8 days after initiating the treatment were as follows: hemoglobin 12.6 (normal range 11.6–14.8) g/dL, direct-form bilirubin 0.2 (normal range 0.0–0.3) mg/dL, total bilirubin 0.5 (normal range 0.2–1.4) mg/dL, and haptoglobin 121 (normal range 30–195) mg/dL. There was no evidence of significant hemolysis. Hemoglobin and bilirubin levels were examined after each chemotherapy treatment and no remarkable changes were observed. After 4 cycles of doxorubicin plus cyclophosphamide, the patient received the first cycle of docetaxel (60 mg/m^2) plus trastuzumab (8 mg/Kg due to the loading dose) 3 months after treatment initiation. Four cycles of docetaxel plus trastuzumab (maintenance with 6 mg/Kg) were conducted. Hemoglobin level was within normal range, and no remarkable changes in the percentage of indirect-form bilirubin were noted. Haptoglobin levels at 4 and 6 months of treatment initiation were 164 and 102 mg/dL, respectively. Adjuvant radiotherapy was initiated after completing chemotherapy. Adjuvant trastuzumab every 3 weeks and tamoxifen 10 mg twice per day was initiated at 6 months after treatment initiation. Till date, there has been no evidence of hemolysis based on laboratory tests, and these data are summarized in Figure 1. The patient agreed of the publication of the case report and she has provided written informed consent.

3. Discussion

The safety of anticancer treatments in patients with G6PD deficiency has never been completely addressed. The first possible hemolytic event after the administration of doxorubicin was reported 35 years ago.[5] However, the relationship between doxorubicin and hemolytic anemia was not definitively confirmed due to the lack of detailed clinical information in that case.

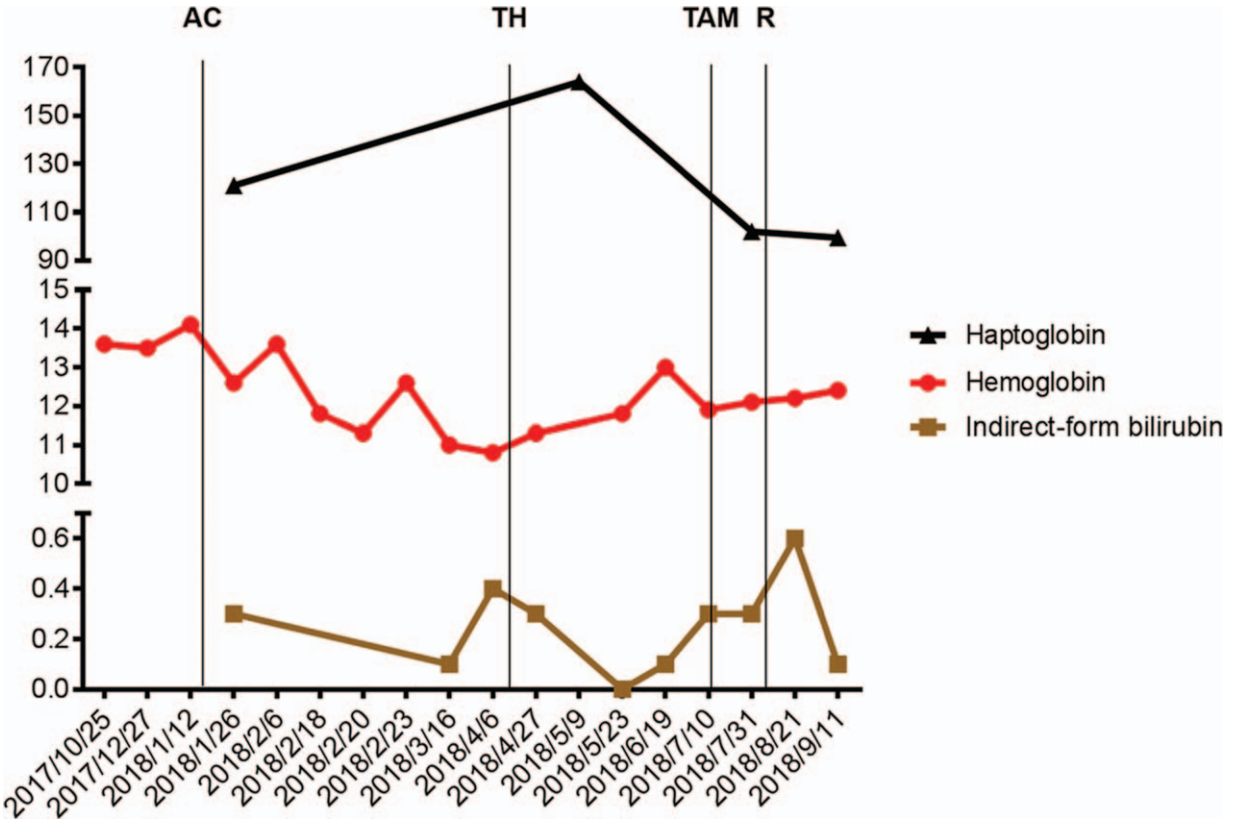

Figure 1. Haptoglobin, hemoglobin, and indirect-form bilirubin levels of the patient during treatments were recorded. Adjuvant therapies included doxorubicin plus cyclophosphamide (AC), docetaxel plus trastuzuamb (TH), tamoxifen (TAM), and radiotherapy (R). Lines represent the first date of each treatment. Normal range: hemoglobin 11.6 to 14.8 g/dL, indirect-form bilirubin 0.2 to 1.4 mg/dL, and haptoglobin 30 to 195 mg/dL.

In another report, although cisplatin was anticipated to induce a high level of oxidative stress, a patient with G6PD deficiency safely completed chemotherapy (bleomycin, etoposide, and cisplatin) for advanced testicular cancer.[6]

G6PD deficiency is an X chromosome-linked disorder. Unlike all hemizygous expression in males, G6PD deficiency in female can be heterozygous or homozygous, but the incidence of the latter is rare.[7] The severity of G6PD deficiency-related hemolytic anemia varies in heterozygous females. It depends on the proportion of G6PD-deficient red blood cells in individuals.[2] There is also limited information available regarding the use of anticancer drugs in females with G6PD deficiency.[4] Different from the ambiguous role of anticancer drugs, rasburicase is contraindicated in patients with G6PD deficiency as it results in severe hemolytic anemia.[8] It is a urate oxidase used to correct hyperuricemia resulting from tumor lysis syndrome.

Breast cancer remains the leading malignancy diagnosed in women. Factors contributing to poor prognosis include involvement of axillary lymph nodes, HER2-positive subtype, and young age.[9] Fortunately, the survival of patients with breast cancer has improved much after introducing chemotherapy, targeted therapy, and hormone therapy. Patients with breast cancer positive for HER2 can benefit from adjuvant chemotherapy and anti-HER2 monoclonal antibodies.[9,10]

Simultaneous detection of breast cancer and G6PD deficiency is anticipated at a location with relatively high incidence of this enzymatic disorder of red blood cells.[11] Appropriate treatment strategies for these patients properly remain unclear. We report a young woman with G6PD deficiency and advanced breast cancer who received all standard treatments without developing hemolysis. Certainly, the risk of hemolytic anemia cannot be ignored in such a population. Therefore, this treatment was given after thorough discussion and with close monitoring of laboratory data. We believe that similar reports of other cases will help clinicians treat these patients confidently.

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Author contributions

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