Primary breast cancer in a patient with Wilson disease

A case report

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Abstract

Rationale: Wilson disease (WD) is an autosomal recessive hereditary disease in which the patient usually has a reduced risk of developing cancer. In particular, with the exception of hepatocellular carcinoma and cholangiocarcinoma, the incidence of cancer is significantly lower in WD patients compared with the general population. This case study presents a rare case of WD complicated with primary breast cancer.

Patient concerns: A 40-year-old woman who was diagnosed with WD at 25 years of age found a lump in her left breast. She has a family history of cancer.

Diagnoses: Ultrasound and mammography results were highly suggestive of a malignant lesion. After core needle biopsy, it was confirmed that she had invasive breast cancer.

Interventions: A modified radical mastectomy was performed for the left breast. As the tumor was defined as a stage IIa triple negative breast cancer, the patient would have been recommended epirubicin/cyclophosphamide + docetaxel for 8 cycles if WD was not a comorbidity. As the patient had cirrhosis and abnormal liver function, she was given paclitaxel weekly for 6 cycles instead.

Outcomes: The patient showed good tolerance, and has not had a recurrence in 2 years.

Lessons: We reviewed the literature for studies of patients with WD complicated with cancers, and to our knowledge, this is the first report on WD complicated with breast cancer. The patient received chemotherapy even with liver dysfunction, which suggests that patients with WD can be safely treated with paclitaxel chemotherapy under close surveillance.

Abbreviations: ATP7B = copper-transporting P-type ATPase, CER = ceruloplasmin, ER = estrogen receptor, HER-2 = human epidermal growth factor receptor 2, K-F ring = Kayser-Fleischer ring, PR = progesterone receptor, WD = Wilson disease.

Keywords: breast cancer, chemotherapy, Wilson disease

1. Introduction

Wilson disease (WD) is a copper metabolism disorder that is caused by a mutation of the gene encoding the copper-transporting P-type ATPase (ATP7B) protein. The clinical manifestations generally include liver cirrhosis, abnormal liver function, extrapyramidal effects, and corneal ring pigmentation such as Kayser-Fleischer (K-F) rings. The patients have increased levels of urinary copper but decreased levels of serum copper and ceruloplasmin (CER). WD complicated with another malignancy is very rare; in fact, WD patients have a significantly lower incidence rate of liver tumors compared with non-WD patients suffering from the same level of liver cirrhosis. Extrahepatic tumors are even rarer among WD patients; we have found only 1 case of WD complicated with colon cancer and 2 cases of WD complicated with acute lymphoblastic leukemia. To date, there has been no report of WD complicated with breast cancer. In this paper, we reported the diagnosis and treatment of a patient with WD complicated with breast cancer.

2. Case presentation

A woman, aged 40, went to see a doctor because of “a lump felt on the left breast more than half a month ago.” A color Doppler ultrasound revealed: a hypoechoic nodule of about 2.0 cm in the outer upper quadrant of the left breast, with a clear boundary, irregular shape, and visible dotted blood flow signals; and enlarged lymph nodes of 2.3 × 0.8 cm in the left subaxillary region, with poor corticomedullary differentiation. A mammography revealed that both breasts had compact mammary glands, with an irregular and isodense mass of 2.0 × 1.5 cm in the outer upper quadrant of the left breast; the mass had an obscure boundary and inhomogeneous interior echoes with no abnormal calcification found and was classified as BI-RADS 4c. The
outpatient clinic carried out a puncture biopsy, and the clinicopathological analysis confirmed that it was an invasive breast cancer. The patient suffered from abdominal distension, swollen legs, glossalalia, and limb jitters 15 years ago, and her CER level was determined to be 0.81 mg/dL; slit-lamp examination revealed the presence of a K-F ring (2+) and abdominal ultrasonography revealed liver cirrhosis. She was diagnosed with WD and received sodium dimercaptosulphonate decoppering treatment (the patient was allergic to penicillamine). With remarkably improved clinical symptoms, she received decoppering treatment on a regular basis thereafter. In 2003, she received a splenectomy due to splenomegaly and hypersplenism. The patient was allergic to penicillin and cephalosporin antibiotics and did not smoke or drink alcohol. She gave birth at the age of 37 without breastfeeding and her menstruation was normal. The patient had a sister who was diagnosed with breast cancer at 42, a maternal aunt who was diagnosed with lung cancer, and a maternal grandmother who was diagnosed with renal carcinoma. No one else in her family was diagnosed with cancer or WD.

Physical examination on admission showed a blood pressure of 126/88 mmHg and a pulse of 83 times/min. She had clear consciousness, spoke fluently, and both eyeballs moved freely without diplopia or nystagmus in any direction. Her limb muscle strength, muscular tension, and tendon reflex were normal. Both upper limbs had a slight postural tremor. The body skin and sclera did not have any obvious yellow staining. Her abdomen was flat and her liver size was normal; the spleen had been resected, shifting dullness (−) was detected, and both lower limbs were not swollen. A 2.0 cm hard enclosed lump was felt in the outer upper quadrant of left breast, with an unclear boundary and poor mobility. A soft swollen lymph node can be felt in the left subaxillary region. Laboratory examination showed a negative hepatitis virus index, hemoglobin levels of 110.4 g/L, blood albumin levels of 38.2 g/L, prealbumin levels of 183.6 mg/L, total bilirubin of 5.8 μmol/L, normal blood coagulation, urinary copper excretion of 840.5 μg within 24 hours, serum copper, serum zinc, copper/zinc. A modified radical mastectomy for the left breast was performed under general anesthesia and the postoperative clinicopathological analysis con...
tumor incidence in WD patients is very low. As for the patient featured in our study, she bears many high-risk factors for breast cancer (advanced maternal age, no breastfeeding, history of malignancy in the family, etc.). We believe that she may be subjected to an even higher risk of tumor incidence if she had not contracted WD and accepted decoppering treatment. There are scarcely any reports regarding chemotherapy risk assessment in WD patients. We could only find 1 case report about chemotherapy for a WD patient complicated with leukemia, where the authors pointed out that full consideration of serious therapy-related toxicity should be taken when treating WD patients with chemotherapy, which mainly includes hepatotoxicity and bone marrow suppression, and that the chemotherapeutic dosage should be reduced when necessary. Since some researchers noted that the ATP7B mutation might result in drug resistance of tumor cells to platinum-based chemotherapy, we adopted taxanes for chemotherapy. The treatment scheme was weekly therapy with paclitaxel, starting from 50% of the conventional chemotherapeutic dose, which was gradually increased to the standard dose (80 mg/m² weekly) while keeping a close watch on the patient’s liver function. According to clinical observation, the patient had good tolerance, with only degree II abnormal liver function and degree I to II bone marrow suppression (reduced glutathione was used as a liver protection drug during this process).

In summary, we reported a case of WD complicated with breast cancer, and to our knowledge, this is the first report on WD complicated with breast cancer. The patient received weekly chemotherapy with paclitaxel for 6 cycles after the operation and we will continue to keep a close watch on the patient.

**Author contributions**

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