

Acute kidney failure and acute pancreatitis was caused after neoadjuvant therapy for a patient with Breast Cancer—a case report

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Abstract

Background: Acute kidney injury (AKI) is a common adverse reaction of platinum drugs in neoadjuvant chemotherapy for breast cancer patients. Approximately 30% of patients receiving cisplatin have acute kidney injury. Carboplatin has less nephrotoxicity than cisplatin as the second-generation platinum compound. There were AKI, nausea and vomiting, acute pancreatitis and oral ulcers occurred in a woman who had intravenous carboplatin in our department.

Case presentation: A 63-year-old Chinese female had neoadjuvant chemotherapy of TCbHP because of diagnosed with stage III breast invasive ductal carcinoma with axillary lymph node metastasis. Fourth day after chemotherapy, she had fatigue and nausea and then suffered from AKI, acute pancreatitis and mouth ulcers. After active treatment in the ICU and breast disease department, the patient's condition improved and was discharged.

Conclusion: Although carboplatin, as a second-generation platinum drug, has less nephrotoxicity than cisplatin, it still needs special attention to avoid damage to the kidneys in clinical citation. At the same time, due to the killing effect of chemotherapeutics on the body's normal immune cells, other abnormal conditions in the body should be paid special attention to avoid more serious consequences.

Introduction

In neoadjuvant chemotherapy for breast cancer patients, acute kidney injury is a common adverse reaction of platinum drugs. Approximately 30% of patients receiving cisplatin have acute kidney injury. Carboplatin is the second-generation platinum compound, which has been certificated to have less nephrotoxicity than cisplatin. One of the mechanisms of cisplatin nephropathy is that cisplatin is taken into the proximal renal tubule epithelial cells via organic cation transporter 2 (OCT 2) on the tubular basolateral membrane, and mitochondrial DNA damage and apoptosis are induced. This article reports a case of acute renal failure caused by carboplatin, followed by acute pancreatitis and oral ulcers and other adverse complications. The reasons for the situation and the prevention and treatment of Chinese and Western medicine are discussed.

At the same time, after cisplatin is deposited in cells, it can cause acute tubular necrosis through inflammation and oxidative stress. In contrast, carboplatin is not transported by OCT 2 and has been suggested to reduce nephrotoxicity due to low tubular accumulation [1, 2]. Till this moment, articles about carboplatin-induced kidney injury are not common. This article reports a case of acute renal failure caused by carboplatin, nausea and vomiting and later adverse complications such as acute pancreatitis and oral ulcers, and discusses the reasons for such situations and how to prevent and treat them with Chinese and Western medicine.

Case Presentation

A 63-year-old female presented to Department of Breast Diseases, Jiangsu Province Hospital of Chinese Medicine, with complaints of discovery of Breast lumps of 6 months duration (Figure 1). The patient denied any special past medical history but the glycosylated hemoglobin is higher than normal after admission (Table 1). In order to clarify the pathological nature of the mass, the patient was performed core needle biopsy (Figure 2) on February 24, 2021, and then diagnosed with stage III breast invasive ductal carcinoma with axillary lymph node metastasis.

Decision of multidisciplinary meeting was to start with neoadjuvant chemotherapy of TCbHP. She received her first cycle of double-targeted therapy with 440mg Herceptin and 840mg Pertuzumab on March 05, 2021 and first cycle of chemotherapy with 110mg Docetaxel and 500mg Carboplatin on March 06, 2021. Then she left the hospital on March 08.

On the second day after leaving the hospital, she felt fatigued, nausea and vomiting 3-5 times a day after eating. The vomit was stomach contents, and diarrhea 4-6 times a day, the excrement initially look yellow and soft, and then turned to yellow watery stool. This condition lasted for 7 days and she did not ask for any system therapy during this period.

The patient went to local hospital and got blood routine examination and blood biochemistry on March 15, 2021 (Table 1). Because of the abnormal test results, she came to our hospital immediately and got some tests again (Table 1). No obvious edema on physical examination. According to her symptoms, physical signs and auxiliary examination, she was diagnosed as "Breast malignancy", "Metabolic acidosis", "Hyponatremia", "Hypokalemia". And then she was treated with rehydration therapy, antacids, hepatoprotective treatment, ECG monitoring, oxygen inhalation, blood glucose monitoring and so on. Then we transferred her to Intensive Care Unit after consulting with ICU and communicating with her family members so that she can get more professional and timely treatment and we can prevent her condition getting worse.

In ICU, she was diagnosed as "Breast malignancy", "Acute renal failure", "Electrolyte disturbance", "Metabolic acidosis", "Hyponatremia", "Hypokalemia", "Stress hyperglycemia" and she was treated with anti-infective, blood sugar regulation, rehydration therapy, anticoagulant, electrolyte balance adjustment, nutritional support. After about 4 days of treatment, the patient recovered gradually (Table 1), and then she was transferred back to Department of Breast Diseases after system evaluation on March 18, 2021.

For the purpose of evaluating the risk of venous thrombosis due to long-term bedridden, necessary imaging studies were performed which revealed abnormal pancreas and peripancreatic adipose space(Figure 3).Investigations revealed increased amylase levels and lipase levels[Table 2].She told us she had suffered from gallbladder stones for about 20 years and eat too much greasy meat recently after we make a detailed inquiry about her medical history. After consulting with department of gastroenterology, we considered that there was a sudden onset of acute pancreatitis in this patient and we treated her with fasting, pancreatic juice secretion inhibition, electrolyte disorders correction, electrolyte balance adjustment. She recovered soon.

Table 1

	2021-02-24	2021-03-08	2021-03-15	2021-03-15	2021-03-15	2021-03-16	2021-03-17
	After the first hospital admission	After the first Neoadjuvant Therapy	Before the second hospital admission	After the second hospital admission	After transfer to ICU		
CRP mg/l		1.10		0.89		164.97	90.34
WBC *10 ⁹ /L	7.63	6.41	17.83	16.26		12.67	11.66
RBC *10 ¹² /L	4.49	4.43	5.12	5.18		4.15	3.89
HGB g/L	130	127	141	144		116	105
NEUT *10 ¹² /L	6.16	6.02	15.84	14.03		11.93	10.50
MONO *10 ⁹ /L	0.16	0.12	0.76	1.77		0.57	0.75
LY *10 ⁹ /L	1.26	0.27		0.45		0.16	0.30
NEUT %	80.7	93.9		86.2		94.1	90.1
MONO %	2.1	1.9		2.8		1.3	6.4
LY %	16.5	4.2		10.9		4.5	2.6
AST U/L	26	29		31		19	38
ALT U/L	53	69		-		27	34
CR umol/L	71.9	61.9	331	204.2		228.5	156.0
BUN mmol/L	5.04	8.2	55.2	59.6		46.45	30.66
UA mmol/L	304	276	983	974		860	478
CK U/L	124		812	780		613	613
CK-MB	178			23		22	
LDH U/L	178		339	1111		312	
GLU mmol/L	6.15	8.63	20.88	23.2		4.22	12.50
GLB g/L	21.6	29.0				16.0	19.7
ALB g/L	46.50	43.0	36	37.0		37.5	35.60
TP	46.50	72.0	-	68.0		55.51	55.27
Na ⁺ mmol	140.5	137.8	120	118		126.7	136.0
Cl ⁻ mmol/L	104.7	103.8	84	89		99	107.4
P mmol/L	0.93	1.15	3.04	3.75		0.97	0.55
Mg ²⁺ mmol/L	1.01	0.88	1.60	1.56		0.80	1.36
K ⁺	3.89	4.52	-	3.45		2.98	3.40

	2021-02-24	2021-03-08	2021-03-15	2021-03-15	2021-03-15	2021-03-16	2021-03-16	2021-03-17
Ca ²⁺	2.39	2.23	-	1.05	0.98	2.27	1.98	
pH			-	7.246	7.368	7.329		
pCO ₂ mmHg			-	17.3	19.7	18.3		
pO ₂ mmHg			-	119.7	245.9	184.4		
HCO ₃ ⁻ mmol/L			-	7.3	11.1	21.0		
SO ₂			-	98.2	99.4			
tHb g/dL					12.2	12.1		
Lac mmol/L				2.22	2.04	1.72		
SBE ⁻ mmol/L					-14.2	-16.5		
ABE ⁻ mmol/L					-12.0			
PCT							6.86	5.04
HbA1c %	6.5		8					

Table 2

	2021-03-15	2021-03-16	2021-03-17	2021-03-19	2021-03-20	2021-03-22	2021-03-23	2021-03-24	2021-03-26	2021-03-29	2021-03-31	2021-04-02	2021-04-05	2021-04-07	2021-04-08
AMS U/L	209	171	444	771	317	117	79	53	89	54	47	41	38	68	67
LPS. U/L	2012	598	1904	1454	580	59	71	54	53	104	78	82	59	474	419

There was another trouble happened to her that the patient started to suffer from dental ulcer with a mass of purulent secretion on March,20,2021. We tested the germ of the purulent secretion and did drug sensitive test which showed Candida albicans infection,then gave her suitable anti-infective treatment.

Take this adverse reaction into consideration, multidisciplinary meeting decided to change the chemotherapy regimen, to use PHP instead of TCbHP. The patient has received 4 cycles of double targets therapy and 4 cycles of chemotherapy without any other adverse reaction until now.

Discussion

TCbHP consists of Docetaxel, Carboplatin, Pertuzumab and Trastuzumab. Carboplatin, a new AnAlogue of cisplatin used in the treatment of breast carcinoma, is the second generation platinum compound, which has been certificated to have less nephrotoxic than cisplatin. The major side effects of Carboplatin are myelosuppression and gastrointestinal effects. Nephrotoxicity, neurotoxicity, hematotoxicity, anaphylactic reaction can also be seen[3].

Firstly, no matter in clinical research or in the researches carried out in the laboratory, there are many reports about the impairment of kidney function even acute renal failure caused by carboplatin[[4-8], which is rare in adverse reactions of the remaining three drugs. Secondly, in the process of recording the medical history, the patient denied the history of diabete, but blood glucose monitoring shows the patient may have diabete(Table 1), which may blow up the drug damage to the kidney at a reasonable dose[9].So we consider that there is the acute kidney injury happened to this patient owing to Carboplatin.

Many experiments show that the metabolism of Carboplatin mainly depends on the kidney, but how Carboplatin causes nephrotoxicity is not fully revealed, which is believed to be owing to both direct and indirect damage to the kidneys including drug absorption and transport, oxidative stress of renal proximal tubule epithelial cells, apoptosis and inflammatory response[10–12]. However, because of the lower nephrotoxicity than Cisplatin, acute kidney injury(AKI) caused by Carboplatin, including acute tubular necrosis can not be seen often[5].

Normally, according to the location and cause of the disease, AKI can be divided into three categories: Prerenal AKI, Renal AKI, Postrenal AKI. Acute kidney injury caused by drug factors may be the main reason of this case. There are three cases reported to be proved acute interstitial nephritis (AIN) by performing a percutaneous renal biopsy[5, 13]. In this case, we focused on the treatment of the condition instead of judgment of the lesion, so we did not perform analogous biopsy to establish an accurate diagnosis.

In order to prevent and handle this emergency situations, we can choose both conventional medication or treatment and traditional chinese medicine treatment and nursing. On one hand, we can use pentoxifylline-non-specific phosphodiesterase inhibitor or pravastatin as adjuvant drugs[13–15]or giving plenty of water adding magnesium to reduce kidney damage[16, 17], and if AKI has happened, we should remove the cause correct electrolyte imbalance or choose symptomatic drugs even alternative therapy. On the other hand, traditional chinese medicine treatment and nursing can also be useful. For example, according to the traditional Chinese medicine“look, smell, ask and cut”on physique screening and judgment, individual guidance for life and health can be carried on to protect kidney. Medicina diet is also suitable for patients to regulate the physique[18]. For example, astragalus carp soup can invigorate the spleen, nourish qi and yin, dispel dampness, promote diuresis, and increase the growth of qi and blood. Carp, adzuki bean, lotus seeds, ginger and other medicines and foods are homologous, so it is safe and effective with long-term consumptio[19]. At the same time, acupuncture point massage at Neiguan point Laogong point Guanyuan point Shenshu point can be good choice for patients, we can choose Shuifen point Yanglingquan point Jianli point as an assistant in edema period[20]. For the low creatinine clearance, retention enema with Serissa foetida Comn Rheum officinale Coptis and Scutellaria baicalensis will be beneficial[21].

Chemotherapy-related nausea and vomiting(CINV)is the most common adverse reactions of Carboplatin, which is one of the middle-to-high grade emetic chemotherapeutic drugs. When the area under the curve is less than 4, the incidence of CINV is 65%[22].Diarrhea is also one of the common adverse reactions of Carboplatin-Docetaxel combination[23]. At the same time, AKI can also been seen nausea, vomiting and diarrhea as its first symptoms[24]. Currently, serotonin receptor antagonists like Tropisetron,Ondansetron,and Granisetron is common and the symptomatic treatment of Traditional Chinese medicine treatment is superior to western medicine in some occasions when it comes to treatment,such as Shenque acupoint can be selected in acupoint sticking therapy with a mixture of cornus officinalis, cumin and ginger juice once a day, the yang deficiency patients can be treated with moxibustion three strong every time[25, 26].

Taking the side effects of these drugs the patient used into consideration[27–31], the symptoms of acute pancreatitis the patient had is more relevant to irregular diet and history of gallbladder stones.

The key reason why chemotherapeutics can treat tumor diseases is that they can inhibit the proliferation of cancer cells and use drugs to inhibit the division of cancer cells. Because chemotherapy drugs are often used systemically, the oral mucosa with similar proliferation characteristics of tumor cells is the first to be attacked[32].The reduced immunity the chemotherapeutics caused, and the reduced barrier function on account of the damage of Oral mucosa cells, which are both in favor of the bacteria or fungi infection[33].

When we discuss the cause of these symptoms, we should take the drugs the patient used and the histories into consideration.

Conclusions

This article reports on a case of breast cancer patient with nausea, vomiting, acute renal failure, acute pancreatitis and oral ulcers and other adverse reactions after neoadjuvant chemotherapy of TCbHp regimen. Through analysis of symptoms, signs, auxiliary examinations and clinical medications, it is believed that the most likely cause of acute renal failure in patients is carboplatin, and how to judge the injury site and how to prevent and treat it clinically is discussed. At the same time, the causes of adverse complications such as nausea, vomiting and oral ulcers caused by chemotherapy and the prevention and treatment of traditional Chinese and Western medicine have been discussed. In this article, the patient’s acute pancreatitis is more likely to have a history of improper diet before admission and a history of gallbladder stones than the side effects of chemotherapy drugs. Through reporting and discussion, clinical treatment can be guided in future treatments.

Abbreviations

AKI
Acute kidney injury
TCbHp
A chemotherapy regimen, Docetaxel combined with carboplatin, combined with trastuzumab and pertuzumab
ECG

electrocardiogram
ICU
Intensive Care Unit
CINV
Chemotherapy-related nausea and vomiting

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

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

Competing interests

The authors declare that they have no competing interest.

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Authors' contributions

TN contributed to conception of the manuscript and writing of TCM characteristic therapy. SL contributed to analysis and drafting of the manuscript. SL made the figure and table. CY revised the manuscript. All authors read and approved the final manuscript.

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Written consent was obtained from the patient for publication of study.

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Figures



Figure 1

Color Doppler ultrasound of breast on February,24,2021

1a A hypoechoic zone about 5.1cm*3.8cm*2.4cm in the upper left breast

Blurred edges, Uneven internal echo and scattered dotted strong echo in the hypoechoic zone and echo attenuation behind the zone.

CDFI: The lesion is of abundant blood flow signals, which show a high impedance.

1b A hypoechoic zone about 1.2cm*0.4cm in the upper left breast

1c Several Oval hypoechoic areas in the left breast axilla one of them is about 2.1cm*0.9cm

Smooth edges, evenly thickened cortex and disappearance of lymphatic hilum structure

CDFI: The lesion is of none flow signals.

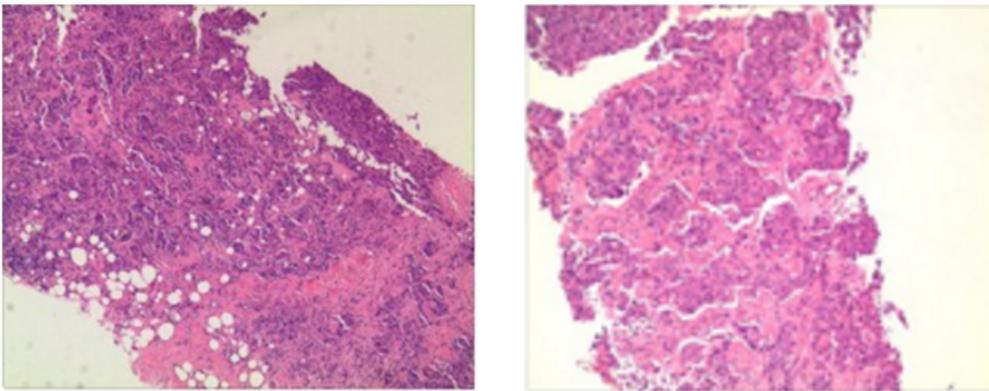


Figure 2

Pathological report of hollow needle puncture on the upper left breast mass and left axillary lymph node

2a Left breast puncture specimen

Pathological diagnosis: Left breast mass puncture specimen Invasive ductal carcinoma Non-special type ,Nottingham classification Level 3 individual vascular tumor thrombus can be seen no clear nerve invasion. Immunohistochemistry showed ER 90%+ PR 1%+ AR 80%+ HER2 3+ Ki67 25% CATA3 3+ P120 (membrane +++),E-cad membrane +++ CK5/6 - Infiltrating cancer cells around the nest calponin(-),P63 - CD31 D2-40 Mark the vessel.

2b Left axillary lymph node puncture specimen

Pathological diagnosis: (Puncture tissue of left axillary lymph node) Invasive ductal carcinoma Non-special type ,Nottingham classification Level 3 individual vascular tumor thrombus can be seen no clear nerve invasion. Immunohistochemistry showed ER 90%+ PR 1%+ AR 80%+ HER2 3+ Ki67 25% CATA3 3+ P120 (membrane +++),E-cad membrane +++ CK5/6 -

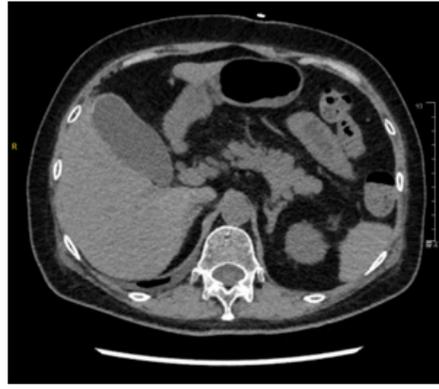


Figure 3

Large pancreatic head, fuzzy peripancreatic fat space, and thickened bilateral prerenal fascia