Discover Oncology

Case Report

Obese patients with malignant tumor: a case series and literature review

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Abstract

Background Pharmacological treatment of malignant tumors in obese patients has been reported from several perspectives. Physiological changes may affect the kinetics of anticancer drugs (e.g., lipophilicity, distribution volume, and metabolism), consequently affecting their efficacy and safety profile. However, specific guidelines for antineoplastic agent dose adjustment according to body weight, mainly due to the under-representation of obese patients in clinical trials, are currently lacking. Moreover, considering that certain tumor development is associated with obesity, the clinical management of obese patients is often complex. We herein report the antitumor treatment options of three obese patients with malignant tumors and review relevant literature to analyze the dosage of antitumor drugs in this setting. This study aims to provide additional data for the clinical treatment of obese patients with malignant tumors.

Case presentation In Case 1, carboplatin was administered at a fixed dose, mainly because of neurotoxicity risk. A maximum creatinine clearance rate (glomerular filtration rate) of 125 mL/min is recommended to prevent carboplatin overdose and toxicity. The maximum carboplatin dose was calculated using the following formula: maximum dose = area under the curve (AUC) × (125 + 25). Methotrexate dose was calculated based on the actual body weight of Cases 2 and 3. While receiving methotrexate, the blood drug concentration was within the reference range (24-h reference concentration ≤ 10 μmol/L), and no serious adverse reactions occurred. As seen in the three cases, considering the particularity of some drugs, for example, more than 90% of carboplatin is excreted through the kidney, carboplatin should be administered at a fixed dose, while other chemotherapy drugs can be administered according to the actual body weight as much as possible according to the patient's condition.

Conclusions The toxicity of chemotherapy has traditionally been assessed based on the actual body weight of obese and non-obese patients. In clinical practice, overweight and obese cancer patients often receive reduced doses of chemotherapy drugs. According to the guidelines set by the American Society of Clinical Oncology, the positive association between the use of chemotherapy and treatment-related toxicity in obese patients lacks evidence. After comprehensive consideration of complications, chemotherapy dose should be determined based on the body surface area(BSA) calculated based on actual body weight, rather than estimated or idealized body weight.

Keywords Obesity · Malignant tumor · Pharmacokinetics · Pharmacodynamics · Chemotherapy

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1 Introduction

A 2017 global adult weight survey published by *Lancet* showed that nearly 90 million individuals in China are obese [1]. Epidemiological studies have linked obesity to increased cancer incidence and mortality [2, 3]. During antitumor treatment, the drug dosage is traditionally determined based on the body surface area (BSA) of the patient. Pathological and physiological changes in obese patients can cause various changes in drug metabolism, such as insufficient tissue perfusion and decreased blood flow due to decreased ventricular function; these alterations may affect the distribution and clearance of drugs [4, 5]. Currently, two methods are commonly used to calculate the appropriate dose of chemotherapy in overweight individuals: (1) limiting the BSA to $2m^2$; and (2) using the ideal weight rather than the actual weight [6].

Retrospective clinical data showed that the current conventional chemotherapy regimen for malignant tumors is often not applicable to obese patients. Evidence from clinical practice shows that up to 40% of obese patients are treated with a limited dose that is not based on actual weight [7]. However, two retrospective studies demonstrated that the toxicity of full-dose chemotherapy is not increased in obese patients [8, 9]. By contrast, empirical evidence indicates that dose reduction in obese patients limits the efficacy, increases the recurrence rate, and leads to a poor prognosis. There are individual differences in liver and kidney functions between obese and non-obese patients. At present, there are few reports on the treatment and management of obese patients. Therefore, we discuss the case data of three obese patients with malignant tumors treated in our hospital and also reviewed related literature. The objective was to provide a reference for the clinical treatment of obese patients.

2 Case presentation

2.1 Case 1

A 31-year-old male patient. In August 2019, the patient was found to have small pulmonary nodules by computed tomography (CT). The patient reported no obvious discomfort at that time, and no special treatment was administered. On March 23, 2020, CT of the lung performed in another hospital showed nodular shadow slightly enlarged in the posterior basal segment of the right lower lung, Therefore, the patient was hospitalized. On March 26, 2020, the patient underwent thoracoscopic resection of the right lower lung nodule plus radical resection of the right lower lung tumor under general anesthesia. During the operation, frozen tissue sections showed invasive adenocarcinoma in the right lung. The lesion invaded the visceral pleura and no lymph node metastasis or intravascular tumor thrombus was observed. Immunohistochemistry: P53 (−), P63 (weak+), Syn (−), CgA (−), TTF-1 (+), Naps in A (+), ki-67 (+, 3–5%). On April 30, 2020, positron emission tomography/CT findings showed no abnormal hypermetabolism in the right lung, pleural effusion in the right side, and pleural calcification in the bottom of the lung and pleural thickening in the right part of the mediastinum and interlobar space. Positron emission tomography/CT imaging of the rest of the body and brain did not show any abnormality.

On May 8, 2020, the patient was diagnosed with invasive adenocarcinoma of the lung (approximately 90% acinar type) with mucinous adenocarcinoma (approximately 10%); notably, a definite vascular tumor thrombus was not found, and the visceral pleura was invaded. On May 11, 2020, and June 8, 2020, the patient received two cycles of postoperative adjuvant chemotherapy with the pemetrexed disodium injection 1.2 g + carboplatin 800 mg. On June 30, 2020, and July 22, 2020, the injection dosage of carboplatin was increased to 900 mg for two cycles. The patient did not have a history of hypertension, diabetes, coronary heart disease, other operations, or blood transfusion. The patient received four cycles of chemotherapy, which was completed without other complaints of discomfort.

2.2 Case 2

A 35-year-old male patient (weight: 105 kg; height: 175 cm) was hospitalized on October 31, 2020, mainly due to weakness in his right limbs lasting longer than half a month. He was diagnosed with a space-occupying lesion in the left basal ganglia. The patient underwent stereotactic needle biopsy on November 4, 2020. Postoperative pathology revealed non-Hodgkin's B-cell lymphoma and a high-grade, large B-cell lymphoma with consideration of the primary center. From November 26, 2020, to May 11, 2021, the patient received nine cycles of chemotherapy with methotrexate 6.5 g (dose 1 [Day1(D1)]) + temozolomide 1,500 mg (D1–D5) capsules. On January 27, 2021; February 9, 2021; and March 10, 2021, the

24-h blood concentration of methotrexate administration was 0.95, 1.2, and 1.3 μmol/L, respectively. On May 10, 2021, head magnetic resonance imaging contrast-enhanced (MRI contrast-enhanced) examination showed that the tumor in the left basal ganglia had further shrunk, and efficacy evaluation indicated partial response.

2.3 Case 3

A 58-year-old male patient (height: 170 cm; weight: 87 kg) was admitted to the hospital on March 11, 2021, mainly due to numbness of the left lower limb lasting for 1 month, weakness of the left lower limb lasting for 2 weeks, and weakness of the left upper limb lasting for 10 days. Following admission, magnetic resonance imaging (MRI) of the head showed that the right parietal lobe was occupied with rich blood supply, accompanied by peripheral edema and lymphoma. The findings suggested perfusion scanning; lacunar infarction of the left cerebellar hemisphere; mild white matter degeneration; there was no sign of stenosis on head magnetic resonance angiogram imaging, and the left transverse sinus was thin. On March 19, 2021, stereotactic biopsy was performed on the right parietal space-occupying lesion under basic anesthesia. The results of the immunohistochemical analysis showed the following findings: cluster of differentiation (CD)3 (−), CD20 (+), CD21 (−), CD30 (−), Ki67 (number of positive cells: 50%), CD38 (+/−), kappa (+), lambda (−), monoclonal, CD10 (−), B-cell lymphoma-2 (Bcl-2) (+), Bcl-6 (+), CD56 (−), MUM1 (+), and C-myc (10% positive). The results of in situ hybridization showed Epstein–Barr virus-encoded small ribonucleicacid (RNA) (−). Immunohistochemistry showed diffuse large B-cell lymphoma of the primary central nervous system. From March 30, 2021, to October 5, 2021, the patient received 10 cycles of chemotherapy with methotrexate 3.0 g/m^2 (D1) plus temozolomide capsule 150 mg/m^2 (D2–6). On April 23, 2021; July 6, 2021; August 5, 2021; November 29, 2021; and December 27, 2021, the plasma concentration of methotrexate was 4.9, 4.46, 6.8, 4.0, and 8.0 μmol/L, respectively. On November 27, 2021, repeated head MRI showed that the abnormal enhancement of the right parietal lobe was slightly larger than that recorded on September 1, 2021. Assessment of the treatment efficacy through imaging indicated stable disease.

3 Literature review

We searched the MEDLINE database (through PubMed) using the keywords "Body Mass Index" (MeSH Terms), or "Body Surface Area" (MeSH terms), and "agents, antineoplastic" (MeSH terms) or "cancer chemotherapy protocol" (MeSH terms) and "Obesity" (MeSH terms). The literature was searched up to December 2023. All included studies involved obese patients with solid tumors who received chemotherapy, studies focusing on systematic evaluation, and economic evaluation were not included in this analysis.

4 Results

In adults, overweight and obesity are determined by the body mass index (BMI). Adults with a BMI in the range of 25–29.9, 30–39.9, and > 40 kg/m^2 (or > 35 kg/m^2 with other comorbidities) are considered overweight, obese, and morbidly obese, respectively.

The Rational Chemotherapy Dose for Adult Obese Cancer Patients suggests that only certain specific drugs (e.g., carboplatin and bleomycin) had to be administered at a fixed dose, mainly due to the neurotoxicity risk [10]. To prevent carboplatin overdose and toxicity, both the US Food and Drug Administration and National Comprehensive Cancer Network guidelines recommend setting a maximum creatinine clearance rate (glomerular filtration rate) of 125 mL/min. Hence, the maximum carboplatin dose was calculated as follows: maximum dose = setting area under the curve (AUC) × (125 + 25). When the AUC was set to 4–6, the maximum dose was 600–900 mg.

According to the formula for the calculation of the BMI = weight (kg)/height (m)^2, the BMI for Case 1 (weight: 123 kg; height 185 cm) was 36.2 kg/m^2; hence, this patient was obese. As the liver and kidney functions were normal, AUC = 6 is set, and the maximum carboplatin dose is 900 mg. There was no occurrence of adverse reactions during chemotherapy.

Case 2 (body weight: 105 kg; height: 175 cm; BMI: 35 kg/m^2) received treatment with 6.5 g of methotrexate according to the actual BSA. The reference range of 24-h methotrexate concentration was < 10 μmol/L. The blood drug concentration was within the reference range, and serious adverse reactions did not occur during chemotherapy. The evaluation of efficacy indicated partial response.

Case 3 (height: 170 cm; weight: 87 kg; BMI: 30.1 kg/m^2) was treated with 6 g of methotrexate according to the actual BSA. The 24-h reference concentration of methotrexate was ≤ 10 μmol/L. The blood drug concentration in the patient during chemotherapy was within the reference range, and serious adverse reactions did not occur. The evaluation of efficacy indicated stable disease. The diagnosis, treatment, and outcome of the three patients are shown in Fig. 1. In Table 1, the data of dose adjustment for obese patients with malignant tumors were collated according to the different chemotherapy regimens used.

5 Discussion

5.1 Treatment effect

Obesity has evolved into a serious global public health problem due to the growing prevalence rate. BMI is a commonly used international standard to measure the degree of obesity and health. An increase in the BMI is associated with some metabolic diseases and an increased risk of developing breast, colon, prostate, endometrial, kidney, and gallbladder cancers [11, 12]. Moreover, obesity affects the pharmacokinetics of antitumor drugs in vivo. Thus, standardization of chemotherapy dosage has become a clinical challenge [13]. In fact, at least eight different methods are available for estimating the weight of obese patients [14]. In this study, we did not focus on targeted drugs and immunotherapy drugs, mainly because a recent meta-analysis demonstrated no effect of BMI on OS or PFS in patients receiving immunotherapy

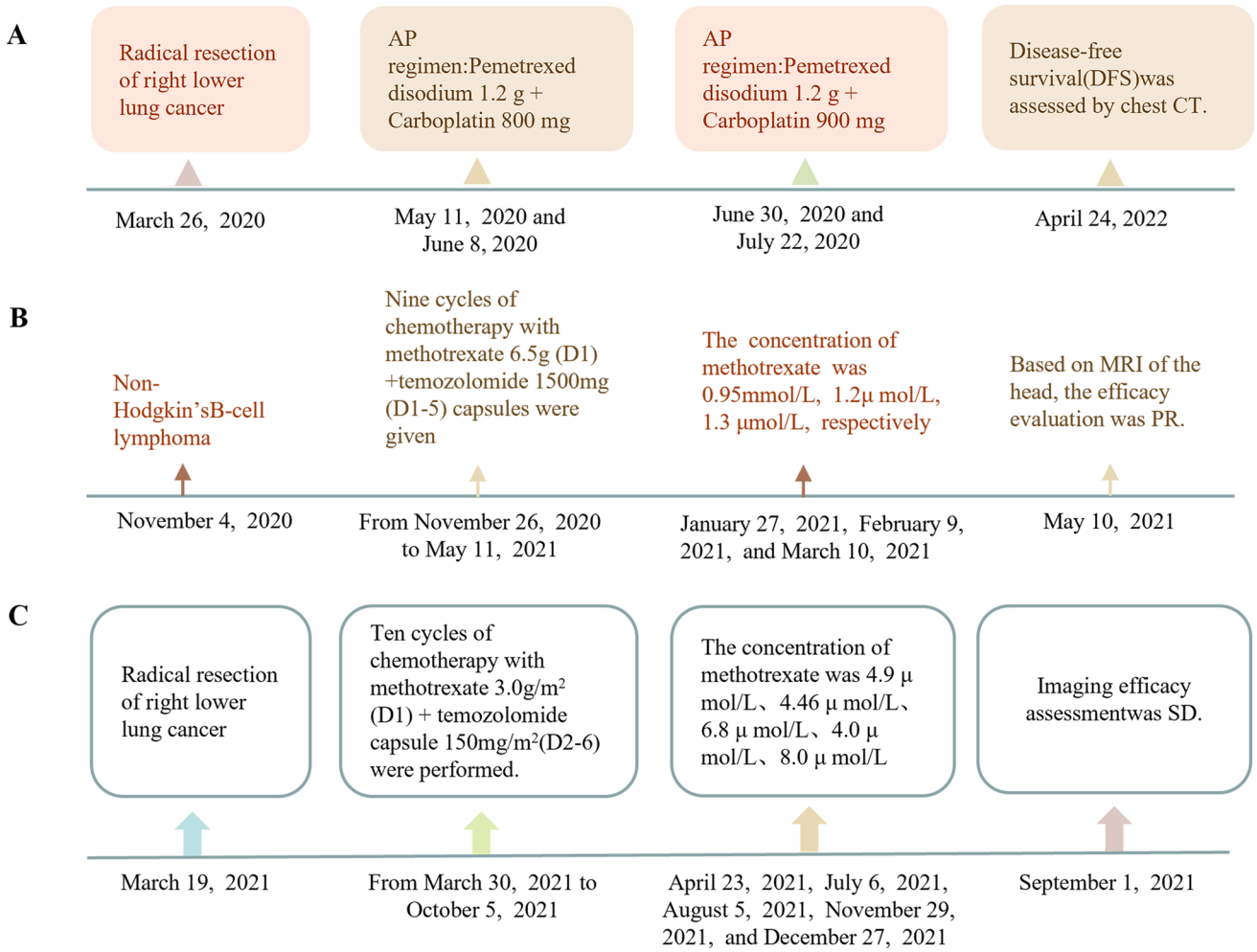

Fig. 1 Timeline of diagnosis, treatment, and regression. **A** Case 1. **B** Case 2. **C** Case 3. *CT* computed tomography, *D1* dose 1, *MRI* magnetic resonance imaging, *PR* partial response, *SD* stable disease

Table 1 Basic characteristics of the included studies

Tumor type	Reference number	Inclusion criteria	Number of obese patients	Chemotherapy regimens	BSA adjustment method	Patients after adjustment for BSA (%)	Results
Breast cancer	Furlanetto [30]	BMI ≥ 30 kg/m^2 Adjuvant chemotherapy	555	Epirubicin × 3 + paclitaxel × 3 + cyclophosphamide × 3 (iddETC protocol) or epirubicin + cyclophosphamide + paclitaxel + capecitabine (EC-TX protocol)	Ideal weight or upper limit of 2 m^2	31%	Higher rate of severe toxicity (actual BSA)
	Morrison [31]	Early-stage breast cancer (stages I–IIIB)	455	Sorubicin + cyclophosphamide (AC) or cyclophosphamide + methotrexate + 5-fluorouracil (CMF) or capecitabine	Drug dose calculated based on BSA		No significant increase in toxicity
	Lote [32]	Early-stage breast cancer	79	Neoadjuvant/adjuvant chemotherapy (5-fluorouracil + epirubicin + cyclophosphamide [FEC], FEC + docetaxel [FEC-T])	Chemotherapy dose was lower than expected	–	Upper dose limit associated with reduced incidence of febrile neutropenia
	Carroll [22]	Non-metastatic breast cancer	114	FEC-T or doxorubicin + cyclophosphamide + docetaxel + trastuzumab (ACTH)	Upper limit of BSA	15.8%	No significant increase in toxicity
	Jenkins [33]	Adjuvant chemotherapy	108	FEC	–	–	No significant increase in toxicity
	Sinicrope [34]	Adjuvant chemotherapy for postmenopausal metastatic breast cancer	173	Anthracyclines + taxanes or anthracyclines only			No significant increase in toxicity
	Colleoni [35]	Non-metastatic pT1–4 lymph node-positive breast cancer	368[b]	CMF (cyclophosphamide + methotrexate + fluorouracil)	Drug dose calculated based on BSA	–	Obesity did not reduce the dose of chemotherapy
	Rosner [9]	Stage II breast cancer with regional lymph node positivity	568	Cyclophosphamide + Adriamycin + fluorouracil	Actual weight	–	Chemotherapy based on actual weight was not linked to a higher risk of toxicity

Table 1 (continued)

Tumor type	Reference number	Inclusion criteria	Number of obese patients	Chemotherapy regimens	BSA adjustment method	Patients after adjustment for BSA (%)	Results
Colon cancer	Stocker [36]	Stage III colon cancer	280	Leucovorin + 5-fluorouracil (LV5FU2) or LV5FU2 plus irinotecan	Upper dose limit calculated based on BSA of 2 m^2	16.10%	The strategy of reduction should be avoided in the adjuvant treatment of colon cancer
	Chambers [37]	Advanced colorectal cancer	870	According to FOCUS, FOCUS2, and COIN trials	Reduced dose (< 5%)	54%	Strategies to reduce the dose of chemotherapy in obese patients with colorectal cancer are not supported
	Meyerhardt [38]	Stage II and III rectal cancer	306	According to Intergroup Trial 0114	Actual weight	-	Obese patients have less toxicity related to adjuvant radiotherapy and chemotherapy, indicating that it is reasonable to administer a fluorouracil dose based on the actual weight of obese patients
	Meyerhardt [39]	Female patients with stages II–III colon cancer	600	According to Intergroup Trial 0089	–	–	Obesity was not associated with increased chemotherapy-related toxicity

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Table 1 (continued)

Tumor type	Reference number	Inclusion criteria	Number of obese patients	Chemotherapy regimens	BSA adjustment method	Patients after adjustment for BSA (%)	Results
Ovarian and endometrial cancers	Meyerhardt [40]	Endometrial ovarian cancer	59	Paclitaxel + carboplatin	Upper dose limit calculated based on BSA of 2 m^2	15%	No statistical difference in toxicity or dose adjustment rate
	Au-Yeung [41]	FIGO stage III/IV Serous adenocarcinoma	70	Carboplatin AUC 5 + paclitaxel	Reduced dose (< 5%)	66%	Lower doses may affect progression-free survival in patients with advanced serous ovarian cancer
	Hansen [42]	Gynecological malignancies	75	Gemcitabine + cationic doxorubicin + paclitaxel	Upper dose limit calculated based on BSA of 2 m^2	–	Compared with the control group, patients with BSA ≥ 2 m^2 in the weight-based chemotherapy group did not experience an increase in non-hematologic toxicity
	Wright [43]	Epithelial ovarian carcinoma	70	Cisplatin + paclitaxel or carboplatin + paclitaxel	–	–	Toxicity of carboplatin was significantly higher in patients with hypertensive ovarian cancer than in women of normal weight; toxicity of the replacement suggests that the patient may be receiving substandard doses of the drug
	Barrett [44]	Ovarian cancer	129	Docetaxel + carboplatin or paclitaxel + carboplatin	–	0%	Patients with high blood pressure and epithelial ovarian cancer did not have a poor prognosis, as long as they received the optimal dose of chemotherapy based on measured GFR and their actual weight

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Table 1 (continued)

Tumor type	Reference number	Inclusion criteria	Number of obese patients	Chemotherapy regimens	BSA adjustment method	Patients after adjustment for BSA (%)	Results
Lung cancer	Georgiadis [45]	Small-cell lung cancer	262[b]	Cyclophosphamide or etoposide + cisplatin, combined with twice-daily chest radiotherapy	Actual weight	–	Obesity at initiation of treatment was not associated with increased toxicity or shorter survival after treatment; there was no support for empirical chemotherapy dose reduction based on ideal weight
	Lam [46]	Non-small-cell lung cancer	67	Two cycles of carboplatin and paclitaxel once every 3 weeks	Actual weight	–	Obesity was strongly associated with improved survival; however, confounding factors were not excluded
Metastatic prostate cancer	Wu [47]	Metastatic disease at the initiation of docetaxel chemotherapy	118	Docetaxel: administered intravenously once every 3 weeks or weekly with some variations in the scheduling of the break week(s)	Attending physician had discretionary power	34.5% (reduced dose)	Empirical dose reduction was not supported for this population
	Cushen [48]	Metastatic desmoplastic prostate cancer	63[b]	Doxorubicin	–	–	Obese patients have a higher overall survival rate than other patients; nevertheless, other factors cannot be excluded
Leukemia	Lin [49]	Acute myeloid leukemia	63[b]	Idarubicin/rubicin for 3 days + cytarabine for 7 days	Based on adjusted body weight	11.1%	Significant differences in complete response rates did not support empirical dose reduction based on obesity
	Wenzell [50]	Acute myeloid leukemia	247[b]	Regular dose of cytarabine for 7 days + anthracyclines for 3 days	Based on adjusted body weight	–	No apparent relationship

AUC area under the curve, *BSA* body surface area, *FIGO* International Federation of Gynecology and Obstetrics, *FOCUS* Fluorouracil, Oxaliplatin, *CPT11* [irinotecan]: Use and Sequencing, *GFR* glomerular filtration rate, *iddETC* intense dose-dense epirubicin, paclitaxel, and cyclophosphamide

Note: all studies were retrospective analyses

[a]Retrospective analysis of the phase III PETACC 3 trial

[b]Total number of patients included in the study

or chemoimmunotherapy, and because the relationship between the effect of targeted therapy and obesity differed according to cancer type and stage of the same cancer [15, 16]; however, obesity was significantly associated with improved overall survival (OS) in patients receiving chemotherapy, but progression-free survival (PFS) was not reached. The association between BMI and OS in patients receiving chemotherapy varied by gender, with an inverse association in men and no association in women [17].

5.2 Specific calculation method for obese patients

There are differences between treatments for the same cancer, which may be attributed to hormone levels, treatment modalities, BMI cutoff point values, and other mechanisms that need to be further explored [11]. To obtain the optimal drug dose and maximum therapeutic effect for the dose of chemotherapeutic drugs in obese cancer patients, it is recommended to select the appropriate drug and dose according to the individualization of patients. After reviewing the literature in this article, several calculation methods are available for obese patients: (1) dose based on BSA: The dose of the most commonly used chemotherapeutic drugs used in clinical practice is calculated using the BSA method, in which the body weight is divided into total body weight (TBW), that is, actual body weight, ideal body weight (IBW), and adjusted body weight (ABW). According to the characteristics of water solubility or lipid solubility of drugs, different body weights are selected to calculate BSA. Because water-soluble chemotherapeutic drugs are difficult to enter the adipose tissue, if TBW is used to calculate the administered dose, the apparent volume of distribution is easily overestimated, which will lead to a large drug dose. ABW is usually used to calculate the administered dose as ABW = IBW + 0.4 (TBW-IBW); fat-soluble chemotherapeutic drugs are more reasonable to calculate the loading dose using TBW due to their strong ability to enter the adipose tissue. Most chemotherapy doses were adjusted based on TBW. (2) fixed dose: based on considerations of neurotoxicity, toxic drugs can be selected according to a fixed dose. For example, the maximum dose of vincristine is limited to 2.0 mg in CHOP (cyclophosphamide, Adriamycin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone) chemotherapy regimen. (3) dose based on area under the plasma concentration–time curve (AUC): dose (mg) = set AUC (mg.min/mL) × [creatinine clearance (mL/min) + 25], as carboplatin. In this study, the dose of carboplatin administered to obese patients in the chemotherapy regimen of Case 1 was calculated based on AUC and maximum creatinine clearance of 125 mL/min, considering that carboplatin is mainly excreted by the kidney, and its renal clearance directly affects AUC. Therefore, renal clearance of carboplatin can be controlled indirectly by controlling AUC, thereby optimizing its toxicity and efficacy. Methotrexate, the chemotherapy regimen in Case 2 and Case 3 was a water-soluble drug, the administered dose was calculated according to TBW in Case 2, and the administered dose was calculated according to ABW in Case 3, and the plasma concentrations in Case 2 and Case 3 were within the reference range, no serious adverse reactions occurred during chemotherapy, and the efficacy evaluation showed partial remission and stability. As shown in Case 2 and Case 3, BSA was calculated according to ABW and TBW, and the plasma concentrations were within the therapeutic window; hence, our findings concluded that BSA could be calculated by ABW and TBW.

5.3 Pharmacokinetics in obese patients

Obesity-induced pathophysiological changes in the body can affect the in vivo process of drugs, leading to individual differences in the effect of chemotherapy and medication risk. Obesity increases cardiac output and blood volume and alters local blood flow, thereby affecting the peak plasma concentration, clearance, and elimination half-life of numerous drugs. Additionally, obesity increases the volume of distribution (Vd) of relatively lipophilic drugs; nevertheless, it does not affect the Vd of non-lipophilic drugs. Drug clearance is typically higher in obese individuals than in those with normal weight, and this is largely controlled by the physiological functions of the liver and kidneys. Moreover, obesity affects hepatic metabolic pathways in different ways. Hepatic metabolism is only slightly enhanced in some obese patients, while it is significantly enhanced in others. However, these changes vary between drugs, and the mechanisms involved in this process are partly understood. For example, obesity increases cytochrome (CYP2E1) activity. However, studies on the effects of obesity on other isoenzymes have reported inconsistent findings. The half-life of the drug is directly influenced by the Vd and is inversely related to clearance; importantly, both Vd and clearance vary in obese patients. With the prolonged infusion of highly fat-soluble drugs, the drug half-life and duration of action may be significantly prolonged after cessation of infusion due to an increased Vd. Therefore, obesity affects the pharmacokinetics of chemotherapeutic drugs and changes the blood flow in the region, thus affecting the distribution and clearance of drugs and consequently affecting the drug exposure of patients. Chemotherapy dose intensity and extension of the chemotherapy interval may cause tumor cells to reduce the uptake of chemotherapeutic drugs, resulting in drug resistance, tumor cell, hence, the

therapeutic effect is unsatisfactory. Studies have shown some differences in the elimination of chemotherapeutic agents between IBW and obese patients. During the development of chemotherapy regimens, dose reduction or dose intensity from standard doses affects DFS and OS in cancer patients [18–20]. Therefore, obese cancer patients should develop chemotherapy regimens based on ABW. Changes in body composition and physiological parameters vary with the degree of obesity and may be influenced by comorbidities commonly associated with obesity, such as diabetes, hypertension, cardiovascular disease, fatty liver disease, or other etiologies. The effect of obesity on pharmacokinetics is shown in Fig. 2.

Obesity is a high-risk factor for many malignancies and associated with worse prognosis in certain types of cancer. In contrast, a higher BMI is also associated with improved prognosis in some cancer types. For example, in patients with metastatic melanoma, obesity is associated with a significant improvement in prognosis [21]. Additionally, studies have revealed a particularly strong association between obesity and hematological malignancies. Similar to the majority of studies on adult patients with acute myeloid leukemia, we did not find any effect of obesity on overall toxicity. Furthermore, consistent with previous evidence, obesity did not affect the response to induction therapy and OS, although approximately 60% of obese patients received upper-dose chemotherapy [22]. Fat can be used as a protective factor to improve the tolerance of patients receiving chemotherapy; however, it can induce resistance to chemotherapy drugs in tumor cells. Accumulating evidence suggests that the decrease in muscle content is related to the poor prognosis of patients receiving chemotherapy [23–25]. However, BMI and BSA cannot completely reflect the proportion of muscle content and fat content, and the selection of chemotherapy dose and the evaluation of patient prognosis are inaccurate. Therefore, a growing number of studies are investigating the skeletal muscle index (skeletal muscle area/height^2) as a criterion for the selection of chemotherapy dosage and assessment of patient outcomes. The relationship among changes in the skeletal muscle index before and after chemotherapy, treatment adjustment, and chemotherapy toxicity has become a future research direction.

5.4 Adverse reactions in obese patients

Numerous chemotherapeutic drugs are characterized by the relatively poor lipid solubility and, therefore, are poorly distributed in the adipose tissue. Fat accounts for a larger proportion of the total weight in obese patients versus those with normal weight. Therefore, obese patients may theoretically receive relatively excessive amounts of fat-soluble chemotherapy drugs. This study presents the results of a retrospective study on the influence of obesity and chemotherapy dose, suggesting that the results are contradictory. The GAIN study demonstrated that patients with breast cancer in whom the dose of chemotherapy was not reduced were at a higher risk of experiencing adverse reactions compared with those who underwent dose reduction [26]. In addition, in several studies, the incidence of agranulocytosis with fever in the upper dose limit group of obese patients was lower than that recorded in other groups [27]. In contrast, four retrospective studies showed that a precise chemotherapy dose did not lead to a higher risk of toxicity [28]. In this population, conflicting data were also reported for progression-free survival and overall survival. Similar contradictory results were observed in two retrospective studies of patients with acute myeloid leukemia [28]. However, in line with the findings of previous studies, we found that chemotherapy doses calculated based on ABW for most patients with malignancies were not associated with a higher risk of toxicity, except for breast cancer, where studies have reported a higher incidence of severe toxicity [26, 30] and that lower doses may affect progression-free survival in patients with advanced cancer [31–50].

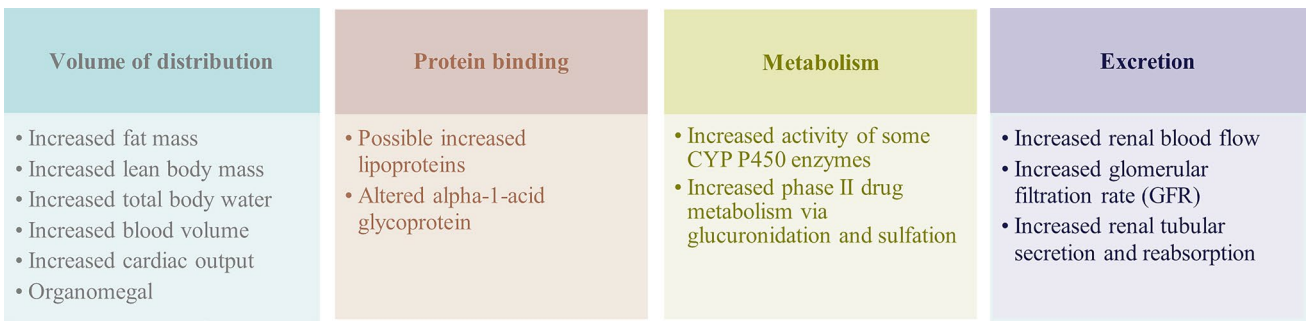

Fig. 2 Effects of obesity on pharmacokinetics. *CYP* cytochrome

Retrospective studies have traditionally evaluated the toxicity of chemotherapy according to the actual weight of obese patients and non-obese patients. In clinical practice, the dosage of chemotherapy drugs for overweight and obese patients with cancer is typically reduced. According to the guidelines established by the American Society of Clinical Oncology, there is no evidence indicating that the use of chemotherapy in obese patients is positively correlated with treatment-related toxicity.

After comprehensive consideration of complications, the chemotherapy dose should be determined according to the BSA calculated based on the actual weight, rather than the estimated or idealized weight. Although further studies are needed, pharmacokinetic studies support the use of actual weight to calculate the dose of most chemotherapy drugs in obese patients [29]. This study presented case data from three obese patients with malignant tumors treated at our hospital and reviewed related literature, with the goal of providing clinical guidance for treating obese cancer patients. Therefore, for drug treatment in obese cancer patients, clinicians and clinical pharmacists should provide personalized medical services suitable for obese patients according to the drug characteristics, combined with the individual conditions of obese patients, underlying diseases, in terms of chemotherapy treatment regimen selection, dose adjustment, and administration methods, to improve the survival rate of patients.

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Author contributions L.P. and Z.MY proposed the direction of research topics, and wrote the first draft of the article; Y.RX., W.X., Y.HY. was responsible for collating case data;Z.Y.and L.J.provided guidance on case data and article writing; S.B. and L.YL. reviewed, supervised, and managed the articles; All the authors approved the final version of the article.

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Data availability statement The original contributions presented in the study are included in the article material. Further inquiries can be directed to the corresponding authors.

Declarations

Conflict of interest The authors declare no competing interests.

Ethics statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This case report was approved by the Medical Ethics Committee of the Fourth Hospital of Hebei Medical University (approval number 2022KS008).

Informed consent to publish Informed consent has been obtained from all subjects and/or their legal guardian(s) for publication of identifying information/images in an online open-access publication.

Consent to participate Written informed consent was obtained from the patient before submission of this article.

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