Heliyon 9 (2023) e18968

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Paraneoplastic syndrome in malignant lymphoma: A case report

Dian Yu [a,b,c,1], Xinyi Tang [a,b,1], Haoyue Xue [b,d], Yongfeng Ao [c], Yongpeng Xie [a,b,d,2,*], Xiaomin Li [a,b,d,**,2]

[a] Lianyungang Clinical College of Nanjing Medical University, China
[b] Department of Emergency and Critical Care Medicine, The First People's Hospital of Lianyungang, China
[c] Clinical College of Guizhou Medical University, China
[d] Lianyungang Clinical College of Xuzhou Medical University, China

ARTICLE INFO

Keywords:
Hypercalcaemia
Lactic acidosis
Diffuse large B-Cell lymphoma

ABSTRACT

Hypercalcaemia associated with malignancy is a complication of advanced tumors. Lactic acidosis is also an extremely rare paraneoplastic syndrome of malignancy, and the presence of both usually indicates an extremely poor prognosis for the tumour. Diffuse large B-cell lymphoma is the most common type of non-Hodgkin's lymphoma and is also a common aggressive lymphoma. It is extremely rare for patients with diffuse large B-cell lymphoma to develop both hypercalcaemia and severe lactic acidosis. In this article, we report a case of CD5 positive diffuse large B-cell lymphoma with hypercalcaemic crisis and persistent lactic acidosis, in which calcium was rapidly reduced to normal after rehydration, diuresis, calcitonin and zoledronate, and continuous renal replacement therapy (CRRT). After correction of acidosis with sodium bicarbonate, diuresis, vitamin B1 and CRRT, the patient's lactate remained at a high level. The aim of this article is to analyse the experience of the combination of hypercalcaemia and intractable lactic acidosis, which should be considered as a serious electrolyte disorder possibly associated with abnormal metabolism of malignant tumors, and to identify and treat the primary lesion as early as possible.

Non-Hodgkin's lymphoma (NHL) is prone to early and distant spread [1]. According to the international working staging of NHL (IWF, 1982), diffuse large B-cell lymphoma is moderately malignant and also a common aggressive lymphoma, the prevalence of which increases with age [2]. Diffuse large B-cell lymphoma often presents with painless, progressive lymph node enlargement and extra-nodal swelling, and may be associated with clinical manifestations such as low-grade fever, night sweats and fatigue. The growth and proliferation of lymphoma and distant metastases can cause haematological and biochemical changes in the body as well as disturbances in the water-electrolyte balance. Hypercalcaemia and lactic acidosis associated with haematological malignancies can be seen in aggressive lymphomas [3]. Reports of diffuse large B-cell lymphoma with hypercalcaemia and lactic acidosis as the first manifestation are rare. The presence of this paraneoplastic syndrome of electrolyte disturbances indicates not only a poor prognosis for the tumour but also a high risk of death.2022 On 12 May, we admitted a 69-year-old woman with a diagnosis of diffuse large B-cell

* Corresponding author. Lianyungang Clinical College of Nanjing Medical University, China.
** Corresponding author. Department of Emergency Critical Care, Lianyungang First People's Hospital, Lianyungang City, Jiangsu Province, 222000, China.
E-mail addresses: ayf970609@stu.njmu.edu.cn (D. Yu), txy118@stu.njmu.edu.cn (X. Tang), xyp8285@njmu.edu.cn (Y. Xie), lyglxm1@163.com (X. Li).
[1] First authors.
[2] Contributed equally.

https://doi.org/10.1016/j.heliyon.2023.e18968
Received 27 November 2022; Received in revised form 12 July 2023; Accepted 3 August 2023
Available online 15 August 2023

lymphoma presenting as a combination of hypercalcaemia and severe lactic acidosis. The patient's basic data and clinical history were collected to summarize the analysis of her diagnosis and treatment.

1. Data analysis

Patient, female, 69 years old, previous history of type II diabetes mellitus for 16 years , Long-term regular oral glucose-lowering drugs dagliflozin and metformin, with fair glycaemic control and usual fasting blood glucose maintained at 4–6 mmol/L. No specific underlying illnesses remaining. In January 2022, the patient began to experience weakness, depression and drowsiness, self-monitoring of blood glucose was not abnormal. Admission glycosylated haemoglobin: 6.0%; ketone bodies (−), six blood glucose results a day: fasting blood glucose 4.4 mmol/L, blood glucose before lunch 5.3 mmol/L, blood glucose 2 hours after lunch 4.4 mmol/L, blood glucose before dinner 4.6 mmol/L, blood glucose 2 hours after dinner 7.7 mmol/L, blood glucose at bedtime 4.4 mmol/L. The spiral CT of the lumbar disc showed lumbar degeneration, wedge-shaped changes in the lumbar 2 vertebrae and bulging discs in lumbar 4–5 and lumbar 5 sacral 1. A lumbar discectomy with lumbar decompression under general anesthesia was performed on April 29, 2022. All preoperative and intraoperative blood gas analyses suggested hyperlactatemia, with continuous monitoring of PH 7.15–7.30 and lactate (Lac) 10.5–12.6 mmol/L (0.5–2.2 mmol/L). Postoperatively, the patient was admitted to the ICU for lactic acidosis and hypercalcaemia, and was treated with respiratory support, fluid replacement and CRRT. The cause of the patient's high calcium and lactic acid was unknown. The calcium was rapidly reduced to normal with haemofiltration treatment and the lactic acid dropped to around 3–4 mmoL/l and CRRT was stopped. He was transferred to the general ward on 5 May, during which time his vital signs were stable, his post-operative recovery was good, his blood calcium was more stable, his lactate was maintained at a low level of increase, and the patient was discharged in a stable condition.

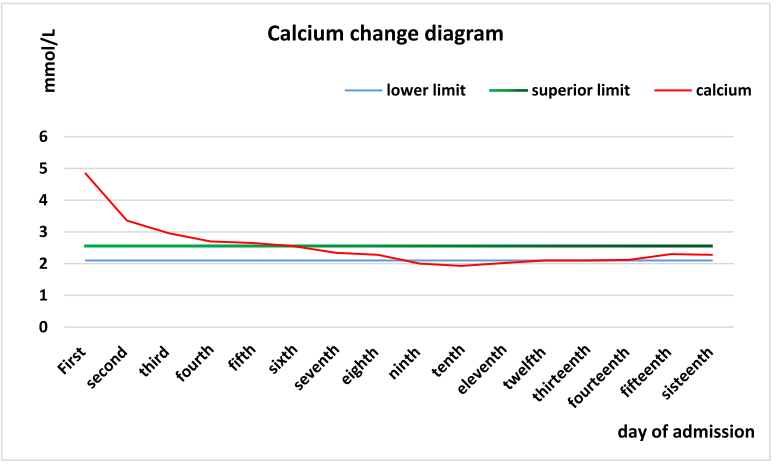
On May 12, 2022, the patient was admitted to the EICU for emergency treatment due to "weakness, depression for more than 4 months, faint consciousness and drowsiness for 1 day", and the initial check of vital signs indicated rapid heart rate, shortness of breath, temperature 38 °C and blood pressure 149/84 mmHg. On admission, blood calcium was 4.86 mmol/L (2.1–2.55 mmol/L), phosphorus 2.38 mmol/L (0.81–1.45 mmol/L); parathyroid hormone 8.27 pg/ml (15–65 pg/ml), blood gas analysis showed PH 7.32, lactate 15 mmol/L (0.5–2.2 mmol/L); white blood cells 37.81 × 10 9/L↑, haemoglobin 91 g/L↓, lactate dehydrogenase: 4285 mmol/L (109–245 mmol/L), Random blood glucose 6.0 mmol/L, urinary ketone bodies (−), considering the patient to be in a critical condition with hypercalcemia and lactic acidosis,a range of therapeutic measures were implemented (Table 1). After rehydration, diuresis, calcitonin and zoledronate, CRRT and other calcium-lowering measures, the calcium rapidly decreased to 2.36 mmol/L. After correction of acidosis with sodium bicarbonate rehydration, diuresis, vitamin B1 and CRRT, the patient's lactic acid remained at a high level (12–15 mmol/L), Changes in blood potassium and lactate are shown in Fig. 1(a and b),. The patient's blood tests were repeated: leucocytes 14.4 × 109g/L, haemoglobin 86g/L, platelets 116 × 109g/L and 23.00% abnormal leucocytes. Bone marrow aspiration and genetic testing was performed and the percentage of abnormal cells was 24.6%, CD4/CD38/ckappa positive, CD45c/CD79a weakly positive, abnormal immune cell phenotype, B cell or plasma cell origin was considered and lymphoma leukemia could not be excluded. PETCT and ultrasound findings suggesting multiple enlarged lymph nodes throughout the body with diffuse increased glucose metabolism in the liver, spleen, and bone marrow (as shown in Fig. 2 ab) were considered malignant lymphoma, and biopsy of the cervical lymph nodes was considered to predispose to CD5-positive diffuse large B-cell lymphoma (as shown in Fig. 3). After continuous treatment in the EICU, the patient's hypercalcaemia stabilised rapidly and the symptoms of acidosis improved, while hyperlacticaemia persisted. R–CHOP chemotherapy was proposed for the treatment of the primary lymphoma.

As shown in Fig. 1(a and b), Graph of the changes in blood calcium and lactate after the patient received EICU treatment on 12 May.

Table 1
Major diagnostic and treatment options and mechanisms of hypercalcaemia and lactic acidosis.

	Treatment measures	Usage and Dosage	Main mechanisms
Hypercalcemia	Intravenous fluid augmentation	0.9% saline and Ringer's solution at 0.5L/h by continuous intravenous infusion	Correction of fluid deficiency, expansion of blood volume and dilution of blood calcium concentration
	Furosemide in combination	20–40 mg micropumped	Used in conjunction with intravenous fluids to increase urinary calcium excretion
	Zoledronate	Intravenous infusion of 4 mg over 15 minutes in 100ml saline	Inhibits osteoclast activity and reduces blood calcium release, especially in hypercalcemia due to malignancy
	Prednisone	60 mg intranasal injection per day for 10 days	Inhibits 1-alpha-hydroxylase and reduces 1,25-dihydroxyvitamin D levels
	CRRT	Low calcium dialysis solution given through haemodialysis	Filters excess calcium ions to lower blood calcium
Hyperlactatemia	Intravenous sodium bicarbonate infusion	250ml 5% sodium bicarbonate by slow intravenous infusion	Neutralizes excess acid in the body, resulting in a balanced acid-base balance
	Vitamin B1	5 mg by intranasal infusion.tid	Vitamin B1 (thiamine) contains thiamine pyrophosphate (TPP), which increases pyruvate dehydrogenase activity and facilitates the efficient use of bioenergy, targeting and correcting the glycolytic metabolic pathway of tumour cells
	CRRT	Lactic acid free, with various electrolytes and sodium bicarbonate dialysate	Removal of excess lactic acid from the body

(a)Graph of blood calcium changes after admission to EICU



(b)Graph of blood lactate changes after admission to EICU

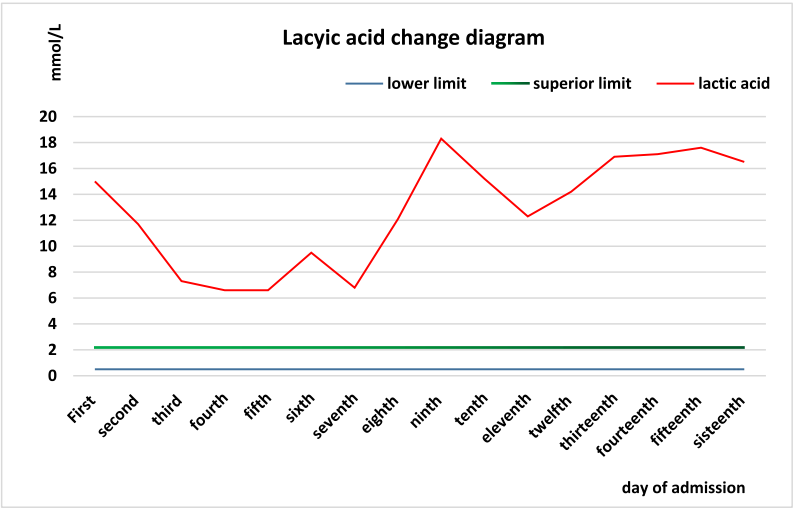


Fig. 1. (a)Graph of blood calcium changes after admission to EICU
(*b*)Graph of blood lactate changes after admission to EICU.

As shown in figure (a): 1. Splenomegaly with increased glucose metabolism, diffuse increased glucose metabolism in the liver, enlarged lymph nodes next to the carotid sheath, supraclavicular region, Bone marrow, hepatoportal area, and next to the great vessels of the retroperitoneum bilaterally, with increased glucose metabolism; consider malignant lesions, with a high probability of lymphoma; 2. No abnormal foci of glucose hypermetabolism in the rest of the body and brain that clearly suggest malignancy; 3. Lacunar cerebral infarction; left maxillary sinusitis; 4. Seen after internal fixation of the lumbar spine.

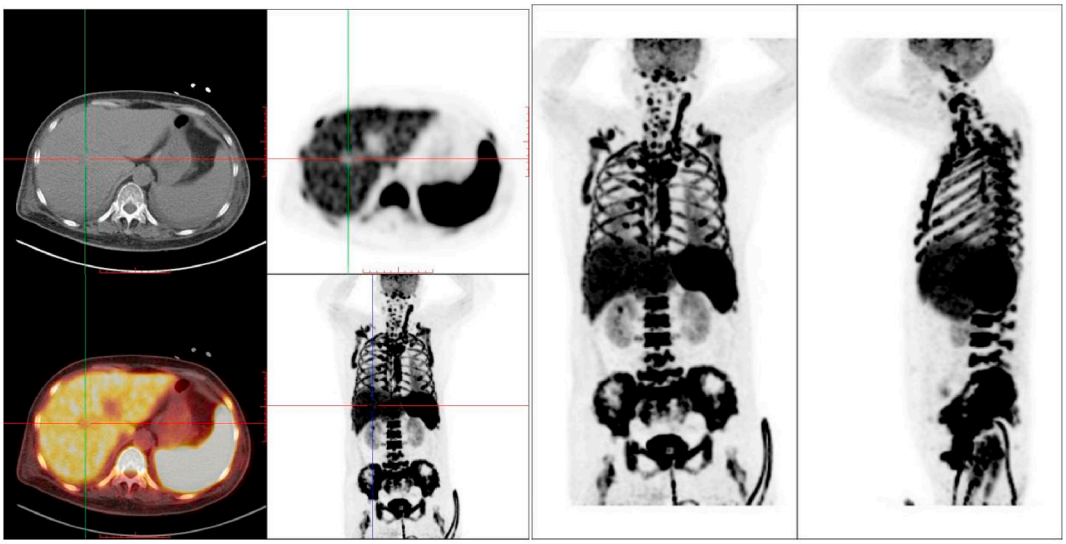
As shown in Fig. 3, Pathology of cervical lymph node biopsy: malignant lymphoma with a tendency towards CD5 positive diffuse large B-cell lymphoma.

CD2 (scattered +), CD5 (3+), CD20 (−), CD79α (diffuse 2+), CD10 (−), BCL-2 (3+), Bcl6 (−), MUM-1 (diffuse 1+), Ki-67 (80%+), CyclinD1 (−), CD23 (−), CD56 (−), CK (−), CD138 (−) CD4 (−), PAX5 (−), CD3 (scattered +), CD34 (−), TdT (−), MPO (−), CD117 (−), CD15 (−), CD68 (scattered +), CD163 (scattered +), ALK (−), CD45 (LCA) (3+), CD20 (repeat -).

2. Management and outcome

During hospitalization in the EICU, the patient's hypercalcemic crisis was treated effectively with fluid rehydration and volume expansion, diuresis, combination of calcitonin and zoledronic acid (single dose 4mg), hormone (60mg nasal infusion 1/day) and CRRT to reduce calcium to 2.36mmol/L within 48h with no significant trend of recurrence. However, the patient's B-type lactic acidosis continued to rise, and sodium bicarbonate rehydration and CRRT to correct the acidity did not have a significant effect. Electrolyte disturbances associated with diffuse large B-cell lymphoma were considered. The patient was then referred to the haematology department for treatment of primary malignant lymphoma with rituximab, cyclophosphamide, doxorubicin, vincristine and

(a) PET/CT whole-body tomographic image (head and body)



(b) Ultrasound of supraclavicular lymph nodes in the neck.

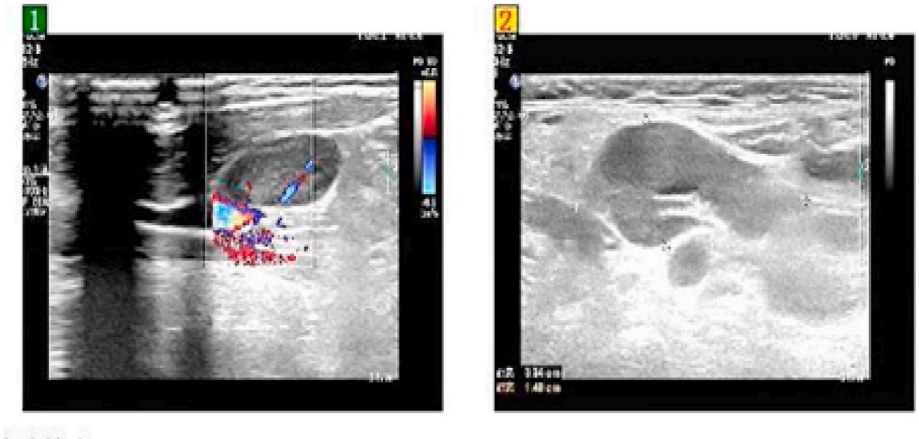


Fig. 2. (a) PET/CT whole-body tomographic image (head and body) (b) Ultrasound of supraclavicular lymph nodes in the neck.

prednisone (R–CHOP). At follow-up, the patient died on June 4, 2022, having abandoned treatment for personal reasons, with a PH of 6.81 and a lactate (Lac) $>$ 15 mmol/L at the time of death.

3. Discussion

The patient in this case is an elderly woman with a 16-year history of diabetes mellitus. First of all, it is not difficult to think that the cause of weakness and depression may be due to excessive blood glucose fluctuations, such as diabetic ketoacidosis, hypertonic hyperglycemic syndrome or mental symptoms caused by hypoglycemia, but the patient's blood glucose were in the normal range and the remaining diabetes-related indicators were not abnormal. In a 69-year-old woman, one should think about the possibility of having a hidden cancer when neurological and psychiatric and psychological diseases are excluded. Especially when electrolyte and blood gas analysis suggest that the patient has almost simultaneous hypercalcemia and lactic acidosis, it should be taken seriously to consider whether it is a paraneoplastic syndrome of cancer and to clarify its primary etiology. During hospitalization, the patient was initially evaluated by routine blood and bone marrow aspiration combined with clinical symptoms, and was considered to have lymphomatous leukemia, which was subsequently diagnosed as $CD5^{+}$ diffuse large B-cell lymphoma with metastases to bone, liver and spleen by whole-body PETCT and lymph node aspiration biopsy. The patient's clinical symptoms and hypercalcemia combined with lactic acidosis were explained.

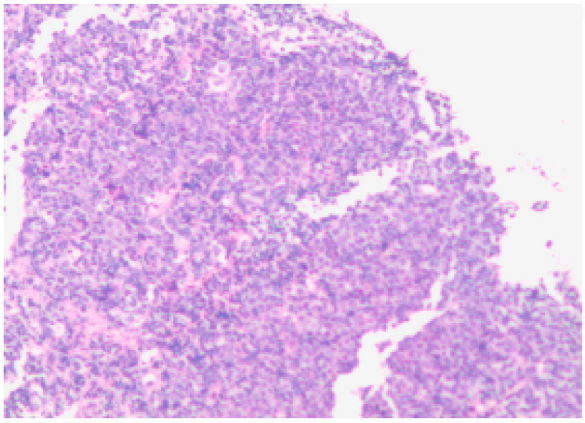


Fig. 3. As shown in figure (b): Bilateral hypoechoic nodules in the neck and left supraclavicular fossa, considering abnormally enlarged lymph nodes.

(1) Hypercalcemia (hypercalcemic crisis)

Hypercalcemia is one of the more common clinical emergencies in the emergency department. There is a dynamic balance of calcium in the body, and hypercalcemia occurs when calcium intake or reabsorption exceeds calcium excretion. The normal range of blood calcium is 2.25–2.75 mmol/L, and hypercalcemia is diagnosed when it exceeds 2.75 mmol/L(4). It usually presents with systemic multisystem symptoms, often manifesting as gastrointestinal discomfort, such as nausea and vomiting; skeletal-related complications, such as bone pain, osteoporosis, and pathological fractures; neurological inattention, weakness, and drowsiness; and cardiovascular system, which may Hypertension and cardiac arrhythmias may occur in the cardiovascular system. When the blood calcium level is $\geq$ 3.75 mmol/L, it is called hypercalcemic crisis, which is a medical system emergency, manifesting as more severe symptoms of hypercalcemia such as lethargy, confusion, irritability, and dehydration, requiring resuscitation [4]. Common causes of hypercalcemia are primary hyperparathyroidism (PHPT), the endocrine effects of malignancy, or drug-related [5]. One of the most common causes is PHPT, which can be identified by measuring parathyroid hormone (PTH) as well as parathyroid imaging. If the patient has low parathyroid hormone levels (such as the patient in the case, whose PTH levels are consistently below normal), malignancy should be suspected as the cause. Asymptomatic hypercalcemia or even hypercalcemic crisis caused by malignancy mostly implies a poor prognosis [6,7]. Hypercalcemia is associated with most cancers, but is most common in solid tumors such as non-small cell lung cancer, breast cancer, multiple myeloma, uroepithelial cancer, or ovarian cancer; non-solid tumors such as lymphoma and leukemia are less common in the hematologic system. The median survival after hypercalcemia in malignant solid tumors is only 52 days (20–191 days) compared to 362 days (18–652 days) for hematologic etiologies, which is seen to be higher in patients with hematologic cancers than in patients with other tumor types [8].

The main causes of hypercalcemia in diffuse large B-cell lymphoma are thought to be: ① Humoral hypercalcemia: malignant tumors can secrete relevant humoral factors through the endocrine system, the most common being parathyroid hormone-related protein (PTHrP), in addition to 1,25-dihydroxyvitamin D and parathyroid hormone (PTH) [9]. PTHrP secreted by tumor cells can act on bone to stimulate bone resorption by increasing the level of the anti-receptor activator of nuclear factor κB ligand (RANKL) and decreasing the level of its inhibitory decoy receptor osteoprotegerin (OPG). In addition, PTHrP and PTH can increase calcium reabsorption in the renal tubules by acting on the kidneys, while 1,25-dihydroxyvitamin D acting on the intestine can increase calcium absorption in the intestine. The synergistic effect of bone, kidney, and intestine causes excessive reabsorption of calcium by the body, resulting in decreased excretion of calcium ions, which leads to hypercalcemia [10].② Localised osteolytic hypercalcaemia: The skeletal system is a common site of metastasis for diffuse large B-cell lymphoma and other cancer cells. Tumour cells can metastasize and infiltrate the bone microenvironment from the primary tumour site and grow and proliferate. Continuously proliferating tumour cells can locally destroy bone, causing bone destruction and lysis by activating osteoclasts, as well as inhibiting bone formation by osteoblasts, releasing large amounts of calcium ions stored in bone, causing hypercalcaemia when the calcium efflux exceeds the excretion levels of the kidneys and liver [11]. In the case described above, the patient's PTHrP and 1,25-dihydroxyvitamin D indicators were not abnormal, parathyroid hormone was below normal levels, and humoral hypercalcaemia was less likely. PETCT suggested that the patient had systemic bone and tumour infiltration in multiple organs, and was accompanied by hepatic and renal insufficiency, which was more likely to be the mechanism of osteolytic hypercalcaemia.

The treatment of hypercalcemic crisis in diffuse large B-cell lymphoma consists of four basic principles: ① Correction of volume deficit: The initial rate and duration of rehydration should be determined according to the clinical symptoms of dehydration, the duration and severity of hypercalcemia, and the patient's underlying disease, especially the presence of cardiac insufficiency. After achieving an adequate rehydration status, a tab diuretic (e.g., tachyphylaxis) may be added as appropriate, but care should be taken to monitor central venous pressure and assess systemic status to avoid serious electrolyte disturbances from the use of diuretics [12].②Inhibit bone resorption: Calcitonin can inhibit osteoclast activity as well as renal tubular reabsorption of calcium and phosphorus, with rapid action, and can rapidly reduce blood calcium concentration; zoledronate and pamidronate can also inhibit

osteoclast activity. It causes apoptosis of osteoclasts to achieve calcium lowering and has a long half-life, so it can be used in combination with calcitonin, with a single dose of 4 mg of zoledronate IV being the preferred regimen [10,13]. When patients cannot take zoledronic acid or have severe renal insufficiency, denosumab, which is not nephrotoxic, can be used, and in a study by Dietzek A, denosumab normalized serum calcium levels in 70% of patients with cancer-associated hypercalcemia [14]. In addition, glucocorticoids may reduce the hypercalcemia associated with 1,25-dihydroxyvitamin D overproduction.③Removal of excess calcium: CRRT or peritoneal dialysis given with low or no calcium dialysate can effectively respond to hypercalcemia crisis and rapidly remove excess calcium. ④Effective treatment of the primary cancer is developed: R–CHOP regimen is mostly adopted for diffuse large B-cell lymphoma.

(2) Refractory lactic acidosis

Lactic acidosis was defined as a serum lactate concentration of more than 5mmol/L, with serum pH < 7.35. Patients often show drowsiness, confusion, delirium, and can also be accompanied by dehydration symptoms such as thirst, vomiting. Lactic acidosis is a serious internal medicine system disease, and its mortality increases with the increase of blood lactic acid level.

When persistent lactic acidosis occurs in a patient with a previous history of type II diabetes mellitus for more than 10 years, the first consideration is whether the chronic poor glycaemic control in diabetic patients has reduced the oxygen-carrying capacity of haemoglobin and localised hypoxia, leading to impaired pyruvate oxidation and lactate metabolism, resulting in lactic acid buildup. However, the patient's blood glucose was well controlled and was in the normal range on rechecking before admission and during his stay, his urine was negative for ketone bodies and his breath did not smell like rotten apples, ruling out diabetic ketoacidosis. Although the patient was on long-term metformin, no medication was administered after admission and blood lactate was consistently maintained above 15 mmol/L. Furthermore, after corrective treatment with CRRT, blood lactate levels did not decrease and the effect of the medication was unlikely. A persistent abnormality in lactate metabolism is currently being considered.

Type B lactic acidosis produced by diffuse large B-cell lymphoma has a unique mechanism. The energy metabolism of tumor cells is different from the aerobic metabolism of normal cells. In the presence of sufficient oxygen, tumor cells will still engage in anaerobic glycolysis, which produces a small amount of energy and lactic acid, promoting the secretion and accumulation of lactic acid. This abnormal metabolism is known as the "Warburg effect "of tumors [15]. Usually persistent lactic acidosis also represents the impairment of the Cori circulation of the liver, suggesting that the tumor has hepatic infiltration and metastasis. This can be verified by liver function test indicators such as lactate dehydrogenase and alkaline phosphatase or by imaging evidence [16]. In most cases, lactic acidosis is a biomarker that indicates an adverse tumor outcome, and its importance as a prognostic indicator can predict potential deterioration, promote more aggressive management, and also help avoid unnecessary treatment [17].

For refractory lactic acidosis, traditional rehydration is currently used in clinical practice for acid correction, but the routine use of sodium bicarbonate infusion to treat lactic acidosis is not supported. In general, sodium bicarbonate therapy shpuld be considered only when the plasma PH < 7.1 or the actual bicarbonate is less than 10mmol/L([18]; [19]). Kallet RH's study mentioned that bicarbonate therapy can improve systemic pH if ventilation and arterial oxygenation are adequate and there is no shock [20]. Pyruvate dehydrogenase (PDH enzyme) is a key enzyme in regulating mitochondrial energy metabolism, which plays a crucial role in the process of aerobic respiration and switches cellular energy production to anaerobic mechanism. Dichloroacetic acid (DCA) can directly or indirectly stimulate the activity of mitochondrial PDH enzyme complex, thereby reducing lactate production. Dichloroacetic acid has been used to treat inherited mitochondrial diseases that cause lactic acidosis by reversing the Warburg effect in cancer cells and restoring the capacity for aerobic glycolysis [21]. Vitamin B1 has a similar and stronger effect than dichloroacetic acid, and can be used to counter the Warburg effect of tumor cells and promote apoptosis of tumor cells [22]. Its mechanism of action is that thiamine pyrophosphate (TPP) is contained in vitamin B1 (thiamine acid), which is an essential cofactor for important metabolic enzymes (including pyruvate dehydrogenase). Supplementation with thiamine can increase the activity of pyruvate dehydrogenase, facilitate the efficient use of bioenergy, and target the correction of glycolytic metabolic pathways in tumor cells [23]. In addition, we also tried to use CRRT, but the treatment effect was not good. At present, there is no exact theoretical basis to prove that CRRT has a significant effect on lactic acidosis caused by malignant lymphoma. However, more and more clinical studies have found that CRRT has a good therapeutic effect on lactic acidosis caused by metformin and other drugs and severe type A lactic acidosis in patients with hemodynamic instability [24,25]. CRRT also has practical and theoretical advantages over traditional intermittent dialysis support and central bicarbonate infusion to improve survival by correcting acidosis, electrolyte changes, and maintaining fluid balance [26].

In the cases of diffuse large B-cell lymphoma analyzed in this paper, after active treatment, the symptoms of hypercalcareous crisis were significantly improved, and the blood calcium was well controlled; the lactate remained at a high level (12–15mmol/L), which may be attributed to the patient's tolerance to high lactate level or progressive Warburg effect. Fundamentally, the management of severe lactic acidosis caused by malignant tumors should focus on treating the primary disease, which in most cases will improve lactic acidosis. Unfortunately, patients gave up chemotherapy for the sake of economic pressure and the critical condition of chemotherapy, and then cause us to think. If the relationship between hypercalcemia, lactic acidosis and haematological malignancies can be quickly considered in the diagnosis of patients at the early stage of the disease, and the targeted treatment of the CHOP program can be carried out in the early stage, whether the survival time of the patients can be prolonged.

4. The conclusion

Although hypercalcemia and elevated lactate are not uncommon in the ICU, our case highlights the greater need for a multivariate analysis of severe electrolyte disturbances that considers not only common etiologies but also other secondary sources, such as

underlying malignancy. The recurrent presence of hypercalcemia and lactic acidosis is an extremely rare paranoplastic manifestation of diffuse large B-cell tumor, suggesting a very poor prognosis and very low survival rate. In addition to the urgent calcitonation measures mentioned above, more research is needed to understand and manage type B lactic acidosis associated with malignancy.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data included in article/supp. Material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e18968.

References

[1] D.A. Arber, A. Orazi, R. Hasserjian, et al., The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia, Blood 127 (20) (2016) 2391–2405. Blood. 2016;128(3):462-3.
[2] A. Smith, D. Howell, R. Patmore, A. Jack, E. Roman, Incidence of haematological malignancy by sub-type: a report from the haematological malignancy research network, Br. J. Cancer 105 (11) (2011) 1684–1692.
[3] K.H. Chan, L. Prabhakar, O. Al-Radideh, B. Okwesili, G. Are, H. Shaaban, A rare case of severe lactic acidosis in a patient with mantle cell lymphoma, J Investig Med High Impact Case Rep 9 (2021), 23247096211034040.
[4] J.J.O. Turner, Hypercalcaemia - presentation and management, Clin. Med. 17 (3) (2017) 270–273.
[5] A.E. Mirrakhimov, Hypercalcemia of malignancy: an update on pathogenesis and management, N. Am. J. Med. Sci. 7 (11) (2015) 483–493.
[6] M.I. Hu, Hypercalcemia of malignancy, Endocrinol Metab. Clin. N. Am. 50 (4) (2021) 721–728.
[7] J. Maletkovic, J.P. Isorena, M.F. Palma Diaz, S.G. Korenman, M.W. Yeh, Multifactorial hypercalcemia and literature review on primary hyperparathyroidism associated with lymphoma, Case Rep Endocrinol 2014 (2014), 893134.
[8] P.J. Donovan, N. Achong, K. Griffin, J. Galligan, C.J. Pretorius, D.S. McLeod, PTHrP-mediated hypercalcemia: causes and survival in 138 patients, J. Clin. Endocrinol. Metab. 100 (5) (2015) 2024–2029.
[9] R.E.O. Ramos, M. Perez Mak, M.F.S. Alves, G.H.M. Piotto, T.K. Takahashi, L. Gomes da Fonseca, et al., Malignancy-related hypercalcemia in advanced solid tumors: survival outcomes, J Glob Oncol 3 (6) (2017) 728–733.
[10] T.A. Guise, J.J. Wysolmerski, Cancer-associated hypercalcemia, N. Engl. J. Med. 386 (15) (2022) 1443–1451.
[11] R.E. Coleman, P.I. Croucher, A.R. Padhani, P. Clézardin, E. Chow, M. Fallon, et al., Bone metastases, Nat. Rev. Dis. Prim. 6 (1) (2020) 83.
[12] M.H. Rosner, A.C. Dalkin, Onco-nephrology: the pathophysiology and treatment of malignancy-associated hypercalcemia, Clin. J. Am. Soc. Nephrol. 7 (10) (2012) 1722–1729.
[13] P. Major, A. Lortholary, J. Hon, E. Abdi, G. Mills, H.D. Menssen, et al., Zoledronic acid is superior to pamidronate in the treatment of hypercalcemia of malignancy: a pooled analysis of two randomized, controlled clinical trials, J. Clin. Oncol. 19 (2) (2001) 558–567.
[14] A. Dietzek, K. Connelly, M. Cotugno, S. Bartel, A.M. McDonnell, Denosumab in hypercalcemia of malignancy: a case series, J. Oncol. Pharm. Pract. 21 (2) (2015) 143–147.
[15] P. Vaupel, H. Schmidberger, A. Mayer, The Warburg effect: essential part of metabolic reprogramming and central contributor to cancer progression, Int. J. Radiat. Biol. 95 (7) (2019) 912–919.
[16] A.H. Sayyed, A. Aleem, M.S. Al-Katari, F. Algahtani, K. Aljerian, T.A. Aleem, et al., Acute lymphoblastic leukemia presenting with liver infiltration and severe lactic acidosis, Am J Case Rep 19 (2018) 453–457.
[17] G.J. Ruan, S. Gandhi, J.P. Abeykoon, S. Schram, T.M. Habermann, B.J. Sandefur, et al., Elevated serum lactate in patients with lymphoma: it is not always infection, Mayo Clin Proc Innov Qual Outcomes 5 (2) (2021) 423–430.
[18] J.A. Kraut, N.E. Madias, Metabolic acidosis: pathophysiology, diagnosis and management, Nat. Rev. Nephrol. 6 (5) (2010) 274–285.
[19] S. Coppola, A. Caccioppola, S. Froio, D. Chiumello, Sodium bicarbonate in different critically ill conditions: from physiology to clinical practice, Anesthesiology 134 (5) (2021) 774–783.
[20] R.H. Kallet, K. Liu, J. Tang, Management of acidosis during lung-protective ventilation in acute respiratory distress syndrome, Respir. Care Clin. 9 (4) (2003) 437–456.
[21] M.O. James, S.C. Jahn, G. Zhong, M.G. Smeltz, Z. Hu, P.W. Stacpoole, Therapeutic applications of dichloroacetate and the role of glutathione transferase zeta-1, Pharmacol. Ther. 170 (2017) 166–180.
[22] N. Ariyoshi, E. Hiraoka, R. Koyamada, Can folate replacement induce lymphoma progression? BMJ Case Rep. 2018 (2018).
[23] W. Manzanares, G. Hardy, Thiamine supplementation in the critically ill, Curr. Opin. Clin. Nutr. Metab. Care 14 (6) (2011) 610–617.
[24] F. Mariano, L. Biancone, Metformin, chronic nephropathy and lactic acidosis: a multi-faceted issue for the nephrologist, J. Nephrol. 34 (4) (2021) 1127–1135.
[25] V. Deepak, S. Neel, A.C. Lohana, A. Tanase, Metformin-associated lactic acidosis successfully treated with continuous renal replacement therapy, Cureus 11 (8) (2019), e5330.
[26] J. Cerdá, A.J. Tolwani, D.G. Warnock, Critical care nephrology: management of acid-base disorders with CRRT, Kidney Int. 82 (1) (2012) 9–18.